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BRITISH MEDICAL JOURNAL

LONDON SATURDAY DECEMBER 11 1948

PROPHYLAXIS OF VIRUS INFECTIONS, WITH SPECIAL REFERENCE TO THE USE OF VACCINES*

BY

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When discussing the prevention of virus diseases we should consider both non-specific hygienic measures and specific prophylactic vaccination. I will not deal with the hygienic aspects, which for some viruses may be more important than inoculation. It may, however, be noted in passing that with regard to some of the more important viruses we are still ignorant of the relative importance of various modes of transmission and therefore do not know upon what hygienic measures to rely. There is still dispute about how the poliomyelitis virus most commonly spreads—by manual or fly-borne contamination or by inhalation. Even in the case of the big group of air-borne upper respiratory infections we know less than we thought we knew some years ago. Are the minute droplet nuclei most important? Or the coarser particles which fall quickly and dry up, and which are then re-dispersed as dust? Or the infected particles spread by the shaking of handkerchiefs and the shaking of hands? I must leave this matter now, except to plead for more fundamental work on modes of transmission as a necessary first step to putting effective hygiene into operation.

Immunity in Virus Diseases

In 1931 I gave a lecture on immunity in virus diseases (Andrewes, 1931). The matter has been discussed many times before and since then, but there seem to be no new principles to bring to your notice. With the old principles you are doubtless familiar enough. Many viruses are conveniently adaptable; patient search and chance have placed in our hands modified viruses attenuated enough to be capable of being used with safety in the living state yet sufficiently unchanged antigenically to give potent and sometimes enduring immunity. Yellow-fever vaccine, which is in this class, sets us a standard to which we would like all vaccines to attain—a single dose which causes no inconvenience, or at most a slight headache, and an immunity so long that we may almost say, "It may be for years, it may be for ever." The modified yellow-fever virus, 17D, now used for making such vaccines, turned up somewhat fortuitously; deliberate attempts to produce another, equally useful, variant virus failed. Lately, so many viruses have been grown and attenuated by growth in fertile eggs that we may hope for more conveniently modified variants to be discovered.

Some viruses can be inactivated, apparently irreversibly, by formaldehyde or other means and still immunize. Large doses must be given in order that enough antigen may be introduced, and these large doses may cause local reactions; a limit may thus be imposed on what can be conveniently given. Immunity after the giving of killed vaccines is much less durable than after the best of the live attenuated vaccines; raised immunity for a year is the sort of result to expect. Formaldehyde is the most generally used inactivating agent, but others, particularly ultra-violet irradiation, are proving to have advantages in some instances. For reasons obscure to us, inactivated vaccines immunize fairly well against some virus diseases—for example, influenza—and very poorly against others—for example, smallpox.

I now turn to discuss two general aspects of virus-prophylaxis: the importance of serological strains of viruses, and the possible application in practice of the so-called interference phenomenon. Influenza affords the best illustration in both instances.

Serological Races of Viruses

We are increasingly forced to realize that many viruses, like many bacteria, have serological races differing enough to affect the results of attempted vaccination. This is true of influenza and poliomyelitis among human diseases. The variations among the influenza and poliomyelitis viruses are far from being understood. Fortunately, variola, yellow-fever, measles, mumps, and some other virus infections are, so far as we know, not apt to vary in antigenic make-up in such a troublesome way. There are two distinct influenza viruses, A and B, believed to be antigenically unrelated to each other: A seems to be the more important. It is within these two groups that minor variations occur to vex us. There are certain classical strains of influenza A studied in laboratories all over the world—the original WS, the PR8, and the Melbourne strains. Whenever in a fresh outbreak new A strains are isolated they are found to differ in serological and cross-immunity tests from these classical strains, and usually, so far as has been tested, from strains recovered from other epidemics. There are always significant cross-reactions, and any two strains may be fairly close together or rather wide apart. Unfortunately there has been no detailed comparison of strains collected from outbreaks in different years in any one country or from different countries in the same year. Therefore we do not know whether there exist limited numbers of types, as with pneumococci and other bacteria, or whether the influenza A virus is capable of an indefinite number of biochemical modifications of a basic structure.

The antigenic variations are important from the points of view of vaccine preparation and of epidemiology. Vaccines have been made in the United States from fluids of infected hens' eggs. In the autumn of 1943 against an A epidemic, and in 1945 against a B outbreak, these vaccines gave most encouraging results. In 1943 the vaccine—in five out of six centres at any rate—apparently reduced the

*Read in opening a discussion in the Section of Pathology and Bacteriology at the Annual Meeting of the British Medical Association, Cambridge, 1948.

incidence of A infection fourfold (Commission on Influenza, 1944). In 1945 a tenfold to twentyfold reduction of B influenza seemed to have been achieved (Francis *et al.*, 1946; Hirst *et al.*, 1947). The 1943 trial was favoured by two factors: first, the epidemic hit the communities under observation only a week or two after the vaccinations; and, secondly, there had been incorporated in the vaccine a very recently isolated strain obtained from a local outbreak in the previous spring. There was a rather rapid assumption that the problem was solved: over 5 million doses of vaccine were given to American troops in 1943–4, and still more in 1945–6. Doubtless the influenza virus chuckled to itself, and quietly mutated to a sufficiently distinct form. At any rate numerous American trials of vaccine in 1947 showed a total absence of protection against the 1947 brand of influenza (Francis *et al.*, 1947). Tests in this country were almost equally discouraging (Mellanby *et al.*, 1948). I have been told that vaccines now being made in the U.S.A. contain recently isolated strains, but I fear that the virus is still chuckling, and that until we know more about its possible range of variation it is useless to produce vaccine on a vast scale. Trials of aspects of vaccine making and testing, other than those concerned with antigenic variants, are of course needed all the time.

Influenza A in America and over here has a 2–3-year periodicity. Influenza B, which is probably a more effective antigen, has a longer, 4–6-year cycle (Commission on Acute Respiratory Diseases, 1946). The fact that the cycles have any regularity at all probably depends on a regular rate of waning of herd-immunity. The periodicity is unfortunately not so regular that we can prophesy with confidence that any particular year will or will not have an influenza epidemic. This lack of precision is perhaps due to this same faculty of the influenza viruses for antigenic variation. If a mutant happens to turn up unusually remote from previous strains it will be able to spread widely and initiate epidemics earlier than would otherwise be the case. In 1945–6 there was good evidence that influenza B was unusually active all over the world, beginning in the mid-Pacific, spreading south to Australia, east to the Caribbean, to North and South America, and later to Europe (*Bull. U.S. Army med. Dept.*, 1945). In 1947 at least one of the novel antigenic types of A which successfully defied the vaccine in America proved to be identical with strains current over here at the same time. All this suggests that the epidemiology of influenza needs to be studied on a world-wide basis.

The World Health Organization has accordingly obtained the consent of the Medical Research Council to set up at the National Institute for Medical Research at Hampstead a World Influenza Centre. This will gather information about the doings of influenza all over the world, and will collect from and distribute to interested laboratories strains of virus. It is hoped that regional influenza laboratories in other countries will collaborate, particularly in collecting local strains, and that we may in time obtain some picture of the behaviour of influenza on a canvas which is really world-wide. If it should appear that new strains are in fact globe-trotters, the possibility exists of anticipating their arrival from abroad and greeting them with really homologous and therefore effective vaccines.

The occurrence of poliomyelitis outbreaks seems related in part to the hygienic conditions of a country and to the opportunities for exposure to virus during infancy. But on top of this is the likelihood that serological variants of poliomyelitis may be spread about, distinct enough to be able to infect people with good resistance to a local strain. The epidemiology of both influenza and poliomyelitis is complex: common to both, as a major cause of the complexity, is the problem of antigenic variation. We have not yet got a vaccine of real promise against poliomyelitis; even if we had one, we should still have to sort out the antigenic variants of the virus.

"Interference" as a Prophylactic Measure

Against a rapidly spreading influenza pandemic of a new type the most rapid vaccine production might well be much too slow. On this account Burnet and Foley (1940) have urged that we should seek attenuated viruses which can be given in the living state by the respiratory route; these could be given in relatively much smaller dose and thus be prepared for large populations much more rapidly. Unfortunately, trials with such attenuated influenza viruses in man have not yet given encouraging results. An approach similar to this involves the attempted practical application of the so-called "interference phenomenon." Virus-workers have known for over a decade that certain viruses will interfere with or suppress the activity of other viruses inoculated at the same time or shortly before. The two viruses may be variants of one species, as in the interference of neurotropic with viscerotropic yellow fever (Hoskins, 1935), or two antigenically related species or even two antigenically unrelated species. Possibly similar effects are dependent on different mechanisms in different instances.

The phenomenon can most easily be studied as it concerns the exclusion of a phage particle from attack upon a bacterium by another phage which has got there first. Apparently even one phage particle can so modify the bacterium, perhaps its surface, perhaps its enzyme equipment, that particles arriving later are unable to enter and have to stay outside and starve (Delbrück, 1945). The phage arriving first can still exclude the one arriving second though the former has been inactivated by ultra-violet irradiation. The phenomenon as regards animal pathogenic viruses is most easily studied in those which grow in the fluids of infected fertile eggs. Is it, one wonders, something of purely academic interest, invented to amuse virus-workers in their laboratories, or does it play a part in epidemiology in real life and can it be applied to the control of disease?

Interference by one influenza virus with another can be shown very readily in infected eggs, but in my experience is much less easily demonstrated in infected mice. Lately my colleague, A. W. Gledhill, and I have been carrying out experiments in ferrets with more success. We used a strain of influenza B which caused practically no fever or symptoms in ferrets. This was given to ferrets intranasally and followed one, two, or three days later with a dose of virus A which produced severe symptoms in control animals. In the B treated ferrets no fever or symptoms developed either from the B or subsequent A infection, and the ferrets were later immune to both viruses. The B by itself induced no true immunity to A, for if the interval between giving the B and the A viruses was extended to a week or more the A infection pursued its normal course or was even worse than usual. The interference is thus effective for a very limited period, presumably while an actual, though inapparent, B infection is in progress. As yet we have been unsuccessful in interfering with an A infection by means of an attenuated A strain. Our results are brought a step nearer to practical application by the finding that B infection also protected ferrets against A when they were exposed for two days to contact with other A-infected ferrets. Controls were readily infected by such contact. These experiments can be repeated regularly, but only within rather narrow experimental limits, and possible practical application depends on the results of much further work. It seems, however, worth while to

draw attention to the possibility of preventing virus disease in the future by means rather different from orthodox immunological methods.

Recent Progress in Prophylaxis of Other Virus Infections

I will conclude with some very brief items of news concerning other viruses not already mentioned.

Mumps.—Mumps virus has now been grown in fertile eggs and has been shown to resemble influenza A and B, fowl-plague, and Newcastle disease of fowls in its ability to agglutinate red blood cells of certain species. These five viruses seem to form a natural group. Like influenza, mumps can be modified by egg-passages, and there are hopes that an attenuated virus suitable for immunization of man may be developed (Enders *et al.*, 1946). Gamma-globulin prepared from mumps convalescent serum has been stated to be of value in preventing orchitis when given early in the disease (Gellis *et al.*, 1945).

Measles.—Measles virus has also been cultivated in eggs, but its presence can be recognized only by transfer back to rhesus monkeys or human volunteers. Egg-passage attenuates it for children, but one cannot yet advocate its practical use for immunization. Its attenuation is not quite enough to satisfy us; on the other hand, the immunity produced is far from complete (Stokes *et al.*, 1943). Prevention or attenuation of measles by immune serum is an old story. It may be noted, however, that for this purpose concentrated gamma-globulin is better than placental globulin (Greenberg *et al.*, 1945).

Rubella.—This has not yet been transmitted to laboratory animals, and the gaining of knowledge about it lags accordingly. Literature is piling up (Editorial, 1947) concerning the occurrence of congenital abnormalities such as cataract in babies born of mothers who suffered from rubella in the early months of pregnancy. Common sense will warn us to shield such mothers at all costs from unnecessary risk of exposure to the disease.

Rabies.—It has been claimed that animals may be experimentally protected against rabies more effectively by concentrated immune rabbit-serum than by traditional vaccines (Habel, 1945). Many people wonder whether, if Pasteurian vaccines do prevent rabies, the effect is not due to something like the interference phenomenon I discussed earlier rather than to immunization in the usual sense. I say advisedly "if" they are effective, for I note with surprise how little notice is officially taken of the late L. T. Webster's (1942) challenge in his book on rabies. He maintained that there was very slender scientific evidence that such vaccines prevented rabies at all when given after infection.

Smallpox.—Experience in the recent war confirms our belief that, because of varying susceptibility and immunizability, vaccination cannot be depended upon to protect an individual, *but* (and may no one quote the first half of this sentence away from its context) vaccination is still a reliable means of preventing and controlling smallpox *outbreaks*, since it will protect most subjects. It has been known for some years that vaccinia grown in tissue cultures or in fertile eggs can be obtained free from all bacteria, and that such a vaccine will immunize man (Buddingh, 1943): but this method of vaccine manufacture has not yet been taken up and seriously tested in comparison with calf or sheep lymph.

Encephalitis.—Viruses cause several forms of mosquito-borne encephalitis in America and the Far East. There is, also, in Russia a tick-borne encephalitis related to the louping-ill of sheep which occurs on the Scottish borders. Against all of these infections formalinized vaccines seem to confer a considerable degree of protection. The cause of sporadic encephalitis in this country is unknown.

The Common Cold.—Work on the aetiological agent at the common cold research unit at Salisbury continues. We have not yet succeeded, as two groups of American workers claim to have done, in growing a virus in eggs. Nor, I need hardly say, have we yet produced a vaccine.

More virus vaccines in the future are likely to be made in fertile eggs. At present yellow-fever vaccine, so grown, is of proved value; so is influenza vaccine within the limits I have discussed. Nearly all the development in this field is going on overseas. I believe that far-sighted manufacturers of biological products in this country would do well to gain experience in this field and contribute their share to its development.

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STREPTOMYCIN RESISTANCE IN PULMONARY TUBERCULOSIS

BY

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Strains of *Mycobacterium tuberculosis* isolated from patients before treatment are remarkably uniform in their sensitivity to streptomycin (Middlebrook and Yegian, 1946; Youmans and Feldman, 1946; Medical Research Council, 1948c). However, during the course of treatment strains often develop a variable degree of resistance to the antibiotic (Youmans *et al.*, 1946; Report to Council on Pharmacy and Chemistry, 1947; Canada, 1947; Hinshaw and Feldman, 1947; Fisher, 1948; Sadusk and Swift, 1948; Medical Research Council, 1948b). A controlled series of cases of pulmonary tuberculosis has been treated with streptomycin under the auspices of the Medical Research Council, and the result of these trials is reported elsewhere (Medical Research Council, 1948a). Among the group of patients receiving streptomycin, 13 were treated at the Brompton Hospital, and from these were obtained sufficiently detailed data on the development of streptomycin resistance to justify a further report.

Method of Investigation

Type of Case.—Patients were aged from 15 to 30 years and suffered from acute progressive bilateral pulmonary tuberculosis of recent origin. Cavitation was present in all. Before treatment 11 had numerous acid-fast bacilli in direct smears of the sputum; 2 had acid-fast bacilli present only in sputum concentrated or in small numbers in direct smears. There were 10 women and 3 men.

Dosage of Streptomycin.—Every six hours 0.5 g. was given intramuscularly. In the earlier part of the trial treatment was continued for six months, but this was later

*In receipt of a grant from the Medical Research Council.

modified to four months. As a result, of the 13 cases 8 had four months' treatment, 3 had between four and five months' treatment, and 2 had between five and six months' treatment.

The *observation period* was six months, except for one patient from whom a resistant strain of *M. tuberculosis* was isolated for the first time during the seventh month.

Clinical Data.—Clinical examinations were made on each patient at monthly intervals and included an *x*-ray examination of the chest. Patients were weighed weekly, except some who were very ill, and the erythrocyte sedimentation rate (Westergren) was measured fortnightly.

Assessment of Clinical Progress.—Each patient's progress was assessed by scoring based on the clinical data and on the temperature. As a measure of *x*-ray progress the independent verdicts of the Medical Research Council panel were taken. Marks were awarded as follows:

	Great Improvement	Improvement	No Change	Worse	Much Worse
Cough		+1	0	−1	
Quantity of sputum		+1	0	−1	
General condition ..	+2	+1	0	−1	−2
X-ray film	+4	+2	0	−2	−4

Temperature: This was based on the average of evening temperatures each month.

Fall from over 100° F. (37.8° C.) to under 99° F. (37.2° C.)	+2
Over 1° F. (0.55° C.) fall	+1
1–2° F. (1.1° C.) rise	−1
More than 2° F. rise	−2

E.S.R.: (In all relevant cases the initial E.S.R. was 40 mm./hour or over):

Reduced to under 50%	+1
Increased by over 100%	−1

Weight changes in a two-months period:

Gain of 10 lb. (4.5 kg.) or over	+3
„ „ 7 to 9 lb. (3.17 to 4.08 kg.)	+2
„ „ 3 to 6 lb. (1.36 to 2.72 kg.)	+1
Loss of 3 to 6 lb.	−1
„ „ 7 to 9 lb.	−2
„ „ 10 lb. or over	−3

No doubt many will differ about the importance allotted to the various clinical observations, but the method does form a basis of comparison between cases, and it provides a clinical scale for correlation with the development of streptomycin resistance in the strains of *M. tuberculosis* isolated.

Degree of Cavitation.—The estimate of the degree of cavitation shown on the initial *x*-ray films was made by Dr. Peter Kerley for the Medical Research Council.

Sputum Examinations.—These were made at short intervals, often twice a week and never less than once a month. During the period at which streptomycin-resistant strains first occurred many cultures failed to grow *M. tuberculosis*, so that the intervals between positive cultures were longer than had been hoped for.

Technique of Testing for Sensitivity to Streptomycin.—The sputum was treated with 4% sodium hydroxide, centrifuged and neutralized, and the deposit inoculated on to Löwenstein–Jensen slopes, which were incubated for nine weeks. The strains of *M. tuberculosis* isolated were subcultured into a synthetic medium containing Tween 80 (Honeywell and Stein, St. James's Square, London) and albumen (Dubos and Davies, 1946), and an inoculum from this was put into bottles of the same medium containing streptomycin. The minimum level of streptomycin inhibiting growth after 10 days' incubation was taken and compared with the level necessary to inhibit a standard strain (H37Rv), which was treated in the same manner. When, for instance, the concentration of streptomycin inhibiting the organism under test was 32 times that inhibiting the standard strain the streptomycin resistance of the test organism was said to be 32 times that of H37Rv. This comparison is taken as the basis of the measurement of the degree of resistance. The technique is fully described elsewhere (Medical Research Council, 1948c).

Degree of Resistance.—In order to obtain comparative figures in analysing our results we have taken the degree of resistance as the average (actually the geometric mean) of all the resistance tests carried out on each case after a plateau level, as described below, had been obtained.

Date of Development of Resistance.—By "date of development of streptomycin resistance" we mean the first day of streptomycin treatment on which a culture was obtained that proved to be four or more times less sensitive to streptomycin than H37Rv. To compare the different cases we have thought it best to take the mean between the last day on which a sensitive culture was obtained and the first day yielding a resistant culture. We have called this the "mean day of resistance development."

Results

Strains Isolated before Streptomycin Treatment.—From most cases two positive cultures were obtained before streptomycin treatment. These strains were either two times less sensitive than H37Rv, two times more sensitive, or equal in sensitivity, except one strain, which was four times less sensitive.

Development of Streptomycin Resistance.—The times taken for resistance to develop and the degree of resistance attained are recorded in Table I, and examples are illustrated in Fig. 1. Certain comments can be made on these results. In all cases there was a period following the beginning of treatment during which the strains of *M. tuberculosis* remained sensitive to streptomycin. In 12 out of 13 treated cases there was later an indication of increased resistance to streptomycin. In 11 out of these 12 the strains were 32 or more times less sensitive. In the twelfth case (Case 82) the strains remained approximately four times less sensitive over a period of more than six months after beginning treatment. Subsequently 1 ml. of an eight-day growth in Dubos–Davis medium of a strain isolated from this case before treatment was started was inoculated into a 25-ml. quantity of the same medium containing 1,000 μg. of streptomycin. From this flask a strain was obtained after six weeks' incubation which, when tested by the technique used in this investigation, was 2,000 times less

TABLE I.—*Degree of Streptomycin Resistance and the Time at which it Developed*

Case No.	Last Day when Sensitive Culture was Isolated	First Day when Resistant Culture was Isolated	"Mean Day of Resistance Development"	Degree of Streptomycin Resistance	Clinical Progress Before Development of Streptomycin Resistance	Clinical Progress After Development of Streptomycin Resistance
87	22	42	32	251·2	− 1	− 2
100	36	42	39	309·2	+ 3	+ 5
86	37	47	42	97·9	+ 6	− 6
92	40	46	43	10,000 or more	+ 5	+ 5
97	35	51	43	10,000 or more	+ 4	+ 5
94	33	61	47	85·1	+ 7	+ 4
99	36	60	48	10,000 or more	− 2	− 7
83	47	49	48	77·6	+ 6	− 1
79	56	76	66	31·6	+ 7	+ 9
95	56	77	66·5	40·7	+ 7	+ 7
82	65	74	69·5	3·4	+ 6	+ 0
89	28	189	108·5	64·0	+ 11	+ 6

The "mean day of resistance development" is the mean day between the last sensitive and the first resistant culture. The "degree of streptomycin resistance" is the average of all the tests done after resistance had risen to a plateau level: the figures are in multiples of the streptomycin resistance of the control strain (H37Rv), and were obtained by taking the antilogarithms of the average of the logarithms of the original figures. The method of assessing clinical progress is described in the text.

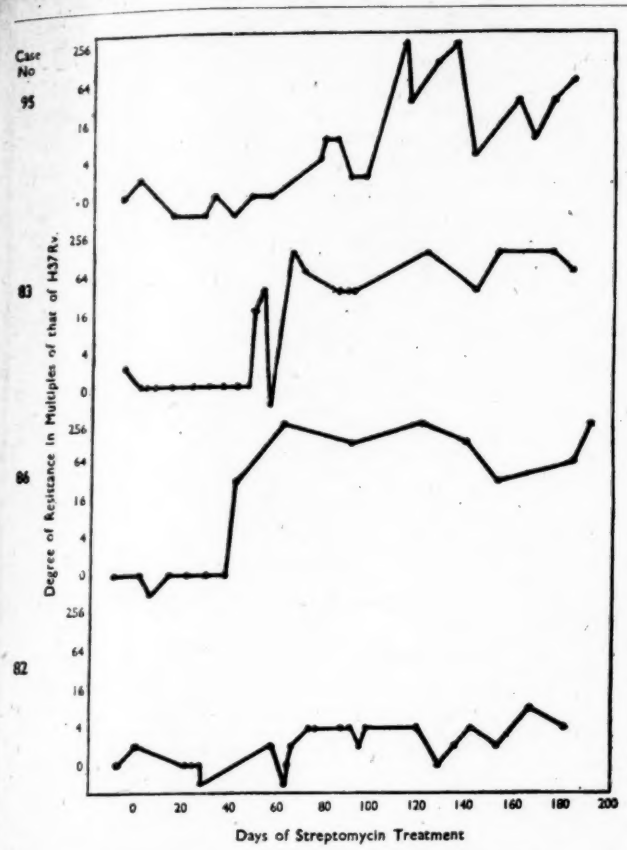

FIG. 1.—Examples of development of streptomycin resistance in cases under treatment. Note that Cases 82 and 95 are included as unusual examples. Cases 83 and 86 are more typical.

sensitive than H37Rv. This work was performed by Miss M. E. Davies at the Postgraduate Medical School of London. It is thus clear that this strain is potentially capable of producing highly resistant variants. The thirteenth case, in which resistance was not observed to develop, yielded a sensitive culture on the 59th day and subsequent cultures were negative. A further case (No. 89) yielded a sensitive culture on the 28th day. Repeated cultures were then sterile till the 189th day, when two grew strains 64 times less sensitive than H37Rv. Since then all subsequent cultures have failed to yield *M. tuberculosis*.

In most cases the level of resistance rose fairly rapidly to a maximum value and then remained at about the same level. After resistance first appeared isolated sensitive strains were obtained in three cases within 15 days, but not after that time. One of these (Case 97) was of special interest. The first resistant culture was obtained on the 51st day of treatment, and was over 4,000 times less sensitive than H37Rv. The sputum was then negative for a fortnight, at the end of which it became blood-stained. This specimen of sputum was noticeably more purulent than previous specimens and contained numerous acid-fast bacilli. On two occasions cultures yielded strains which were sensitive. After this the sputum became negative by smear and culture, and has remained so for a further 14 months.

Streptomycin resistance was observed to develop in cultures from three patients whose sputa subsequently became negative (Cases 79, 89, and 97).

Numbers of Tubercle Bacilli in the Sputum and Development of Resistance.—Fig. 2 shows that, if bacilli persisted in the sputum, in most cases the number diminished under treatment to a minimum occurring at or after the time that resistance developed. After this the number again increased.

Additional Notes on the Development of Resistance.—In one case (No. 92) sensitive tubercle bacilli were cultured from urine after more than three months' treatment and after the strains from the sputum had been consistently highly resistant for six weeks. In Case 99, dying eight days after finishing treatment and whose sputum cultures had been at least 4,000 times less sensitive than H37Rv, 18 cultures were taken post mortem from different parts of the lungs and all showed the same high degree of resistance.

In two cases resistance tests were done on individual colonies from cultures which routine tests had shown to be resistant. In the first case (No. 92) the culture was the first one shown to be resistant, and was obtained seven days after the last one known to be sensitive. By the routine test the culture was 128 times less sensitive than H37Rv. The growth was a heavy one, and from it nine colonies were selected and tested individually for sensitivity. Four were of the same sensitivity as H37Rv, two were four times less sensitive, two were 64 times less sensitive, and one was 128 times less sensitive. In the second case (No. 94) the culture was the second one shown to be resistant. It was obtained 33 days after the first resistant culture and 61 days after the last sensitive one. Growth was moderate, and the culture was 64 times less sensitive than H37Rv by

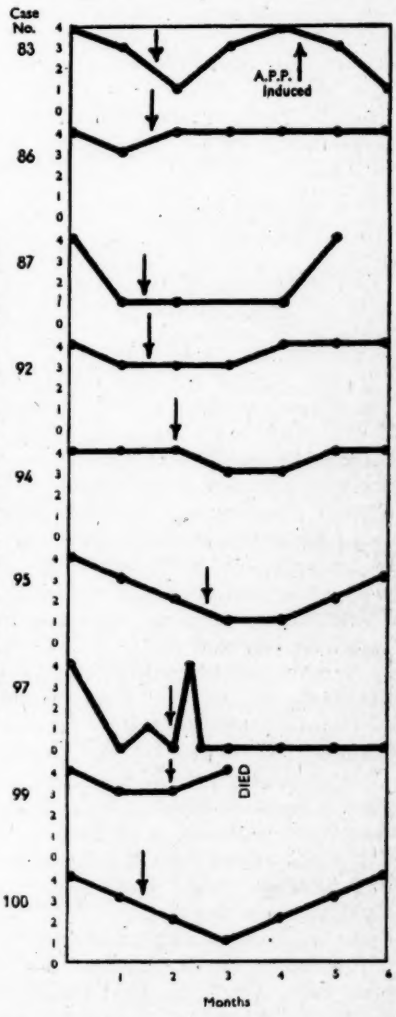

FIG. 2.—Degree of positivity of sputum in relation to development of streptomycin resistance. Ordinates indicate degree of positivity, 0=negative to smear and culture; 1=culture only positive; 2=positive on concentration; 3=moderately positive on direct smear; 4=strongly positive on direct smear. The arrows indicate when the first resistant culture was obtained. The monthly positivity figures are based on three examinations in most cases. Other results are indicated only where they are important.

the routine test. Fifteen colonies were selected for individual testing. One was 16 times, 5 were 32 times, 8 were 64 times, and one was 128 times less sensitive than H37Rv. It is of interest that in this case, where the culture was obtained at least a month after resistance had developed, a

higher proportion of the colonies were resistant than in the first case, where the culture was the first one shown to be resistant.

Analysis of Results

An attempt was made to correlate the mean day of development of resistance, the degree of resistance attained, and the clinical progress both before and after the development of resistance. Using the system of scoring previously described, Spearman's rank correlation coefficient was calculated and a test of significance applied, making the appropriate adjustment for the small number of cases. Student's $t=\rho\sqrt{\frac{n-2}{1-\rho^2}}$ (Kendall, 1943). The results are indicated in Table II. This coefficient was used rather than the usual correlation coefficient, since it seemed possible that the degrees of resistance developed were not arranged in a normal distribution. One of the determinations of the mean day of development of resistance was obtained only within very wide limits (Case 89). Two sets of figures are given, one excluding and the other including this result. There was an apparent relation between the mean day of resistance development and the clinical progress before development of resistance if the values include results from this case. If, however, these results are not included the correlation coefficient is only suggestively high. Cases which did poorly developed resistance early (Fig. 3).

TABLE II.—*Correlation of Streptomycin Resistance of Tubercle Bacilli with Certain Factors*

Correlation between	Cases, including Case 89		Cases, excluding Case 89	
	Correlation Coefficient ρ	Probability of Occurrence by Chance	Correlation Coefficient ρ	Probability of Occurrence by Chance
Progress before resistance development and mean day of resistance development	**0·6713**	**0·02–0·01**	0·5727	0·1–0·05
Progress after resistance development and mean day of resistance development	0·4056	0·2–0·1	0·2727	0·4–0·3
Progress before resistance development and degree of resistance	**−0·7133**	**0·01–0·001**	**−0·7091**	**0·02–0·01**
Progress after resistance development and degree of resistance	−0·3497	0·3–0·2	−0·2182	0·6–0·5
Mean day of resistance development and degree of resistance	**−0·6748**	**0·02–0·01**	**−0·6318**	**0·05–0·02**
Progress before resistance development and progress after	**0·6014**	**0·05–0·02**	0·5182	0·2–0·1
Average temperature before treatment and mean day of resistance development	−0·2815	0·4–0·3	−0·1932	0·6–0·5
Average temperature before treatment and degree of resistance	0·5000	0·1–0·05	0·4796	0·2–0·1
Degree of cavitation and mean day of resistance development	−0·3776	0·3–0·2	−0·2273	0·5–0·4

Note.—Correlation coefficients in bold type are considered statistically significant, since the probability of their occurrence by chance is less than the conventional 1 in 20.

There was a definite relation between the clinical progress before resistance developed and the degree of resistance that eventually occurred (Fig. 4). Those cases doing well in the early stages of treatment developed a low degree of resistance, while those doing poorly produced more highly resistant organisms. This correlation was significant. There was also a significant correlation between the mean day of resistance development and the degree of resistance eventually achieved. The higher the degree of resistance the more rapidly did it appear (Fig. 5).

There was no significant correlation between the mean day of resistance development or the degree of resistance that developed and the clinical progress after that development; nor was there any demonstrable relation between the time at which resistance developed and the general condition on admission as assessed either on general clinical grounds or as the average evening temperature before treatment was begun. A "dot-diagram" suggested a possible relation between the degree of resistance and the average evening temperature; those with higher average temperatures tended to develop higher degrees of resistance, and vice versa. This relation was not, however, statistically significant. There was no significant relation between the mean day of resistance development and the extent of cavitation before treatment, though there was some suggestion that those with lesser degrees of cavitation developed resistance later, and vice versa. No relation could be shown between the degree of resistance and the extent of the cavitation. Our failure to demonstrate these relations is not, however, conclusive, owing to the small number of cases.

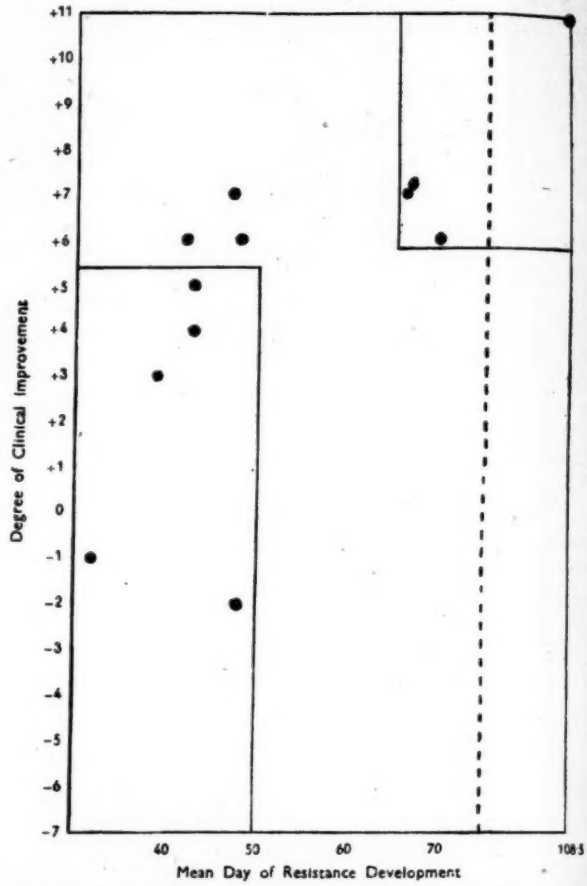

FIG. 3.—Relation of mean day of resistance development to clinical progress before resistance had occurred. The "boxes" indicate the main groups into which the cases fell.

Clinical Effect of Resistance Development.—The clinical progress of our individual patients during their streptomycin course, before and after the development of resistance, is shown in Fig. 6. It will be seen that in only two cases did any great change in the clinical course coincide with the first demonstration of streptomycin resistance (Cases 83 and 86). In Case 82, in which there was an apparent change, resistance did not rise above four times that of H37Rv during the relevant period. Two cases which went downhill from the start (Nos. 87 and 99) perhaps showed some slowing in the deterioration before resistance developed and thereafter deteriorated more rapidly, but one cannot say that this acceleration might not have occurred if no streptomycin had been given.

Factors other than Streptomycin Resistance which may affect the Response to a Course of Streptomycin.—As we have not in most of our cases been able to demonstrate

a close relation between the development of resistance and the subsequent clinical course, we have considered what other factors might be involved. Two obvious factors are persistent cavitation and the patient's own defences. This latter factor is very difficult to assess, but we have attempted a rough estimate by comparing the patient's progress before streptomycin treatment with the extent of his disease as shown radiologically. We have tried to assess for each patient the relative importance to the outcome of the streptomycin course of residual cavitation, the patient's own defences, and, where it occurred, streptomycin resistance. Such an estimate can, of course, be only very rough, but it may serve to suggest the different factors involved.

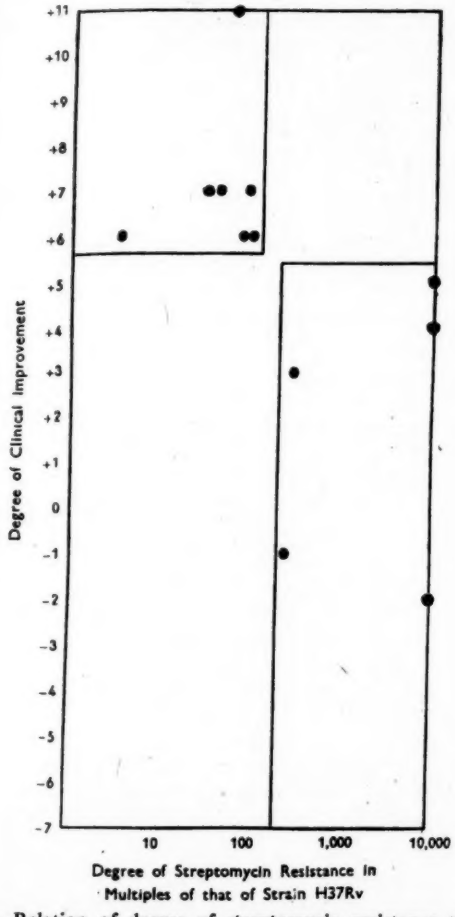

FIG. 4.—Relation of degree of streptomycin resistance to clinical progress before resistance occurred. The "boxes" indicate the groups into which the cases fell.

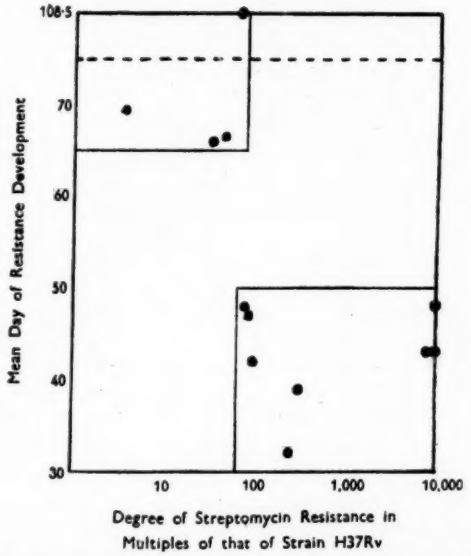

FIG. 5.—Relation of degree of streptomycin resistance to mean day of resistance development. The "boxes" indicate the groups into which the cases fell.

In three of the eight cases doing well the patient's own defences were thought to have contributed significantly. In four, however, residual cavities made the ultimate outlook doubtful. In the seven cases whose organisms developed streptomycin resistance this did not seem to have affected the issue.

Of the five cases doing relatively badly the development of streptomycin resistance was of obvious importance in two and residual cavitation of importance in one of these and in three others. In two cases streptomycin treatment seemed to have resulted in a slight degree of improvement, in two we thought it had perhaps retarded a downhill course, and in one we were unable to attribute to it any significant benefit.

Discussion

Theoretically there seem to be two possible mechanisms by which strains of tubercle bacilli resistant to streptomycin might appear in the sputum. On the one hand the entire surviving bacterial population might become gradually adapted to growth in the presence of the drug. On the other hand the patient's population of tubercle bacilli before treatment with streptomycin might contain organisms with varying degrees of resistance, the more highly resistant being few in number. Under treatment these would have an advantage over the sensitive strains and might gradually come to replace them.

The first hypothesis presupposes that all strains of tubercle bacilli are initially of equal sensitivity to streptomycin but are capable of gradually adapting themselves to growth in its presence. This adaptation would be most likely to occur if the organisms were exposed to concentrations of streptomycin small at first but gradually increasing. Such conditions would exist if there were parts of the lung, such as cavities, in which streptomycin did not act. Radiating from these areas there would be gradients of antibiotic activity, and strains of tubercle bacilli initially sensitive might little by little grow outwards from the protected areas as they became adapted to higher and higher concentrations of streptomycin. In its pure form this hypothesis is improbable. Not only has such a mechanism been excluded in the development of resistance to penicillin (Luria, 1947) but Pyle (1947) and Davies (personal communication—1948) have shown that strains of tubercle bacilli isolated from the sputum before treatment are not of uniform streptomycin sensitivity; if sufficiently large inocula are used strains highly resistant to streptomycin can be obtained.

If the other hypothesis is correct and streptomycin-resistant organisms come to dominate the patient's population of tubercle bacilli by a process of selection of a few strains innately resistant, we need not presuppose gradients of antibiotic activity. Nevertheless if there were areas relatively protected from the effects of streptomycin, in these the general population of tubercle bacilli would continue to increase and there would therefore be more chance of resistant strains emerging. In addition it might be that gradients of antibiotic activity favoured the growth of moderately resistant strains, and that in these strains selection of highly resistant forms was more likely to occur. Whether such gradients exist is of practical significance; for only if they do is it worth while searching for streptomycin derivatives with a greater diffusibility or a greater activity at low *p*H.

There is no direct evidence that there are gradients of streptomycin activity in certain areas of the tuberculous lung, but observations have suggested that streptomycin resistance occurs more readily under the physical conditions associated with human pulmonary tuberculosis. Streptomycin-resistant organisms are rarely isolated from treated cases of tuberculous meningitis. Of 15 cultures obtained from the Medical Research Council series after the second month of treatment only three showed a rise in streptomycin resistance (Medical Research Council, 1948b). The technique of estimating the degree of resistance was identical with that described in this paper, and in a number of cases the strains were retested by one of us. In guinea-pig tuberculosis treated with streptomycin the development of drug resistance has so far been reported in only two of the many experiments carried out (Feldman *et al.*, 1947, 1948). The contrasting findings might be due to the existence in human pulmonary tuberculosis of foci of bacilli in caseous areas or cavities less readily penetrated by streptomycin, though in tuberculous meningitis there are often regions isolated by fibrous tissue from the streptomycin circulating in the cerebrospinal fluid (Smith *et al.*, 1948). Another, and perhaps more probable, explanation is that the local aggregates of bacilli tend to be larger in human pulmonary tuberculosis, thus increasing the chance of a resistant strain being present.

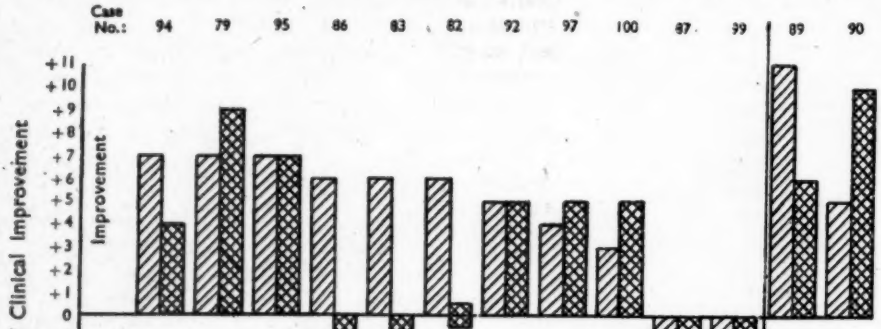

FIG. 6.—Clinical progress before and after development of streptomycin resistance. The figure covers a four-months period from the beginning of streptomycin treatment. With Case 89, in which resistance was shown to have developed only on the 189th day, and with Case 90, in which the sputum became negative before resistance occurred, clinical progress in the first two months is compared with that in the second two months.

There is also some evidence that streptomycin does in fact penetrate cavities. Steenken and his colleagues (1947) found a concentration of streptomycin averaging 7.7 μg./ml. in fluid from Monaldi drainage, the average blood concentration being 13.3 μg./ml. In our experience the strain H37Rv is inhibited by about 1 μg./ml. when growing in Dubos–Davis medium adjusted to *p*H 6, so that it seems likely that the streptomycin concentration in cavities is adequate for bacteriostasis in spite of the acidity of tuberculous pus. It must be remembered that Steenken's figures relate only to a type of cavity suitable for treatment by Monaldi drainage. Schwabacher (1948), however, claims that sputum inhibits the action of streptomycin; in addition, it may be that tubercle bacilli are unaffected by streptomycin when growing within cells (Barski, 1948).

If bacteriostatic levels of streptomycin are attained within cavities the continuing isolation of sensitive bacilli from the sputum in the early stages of a course of streptomycin might be due to the presence of dormant viable organisms which are coughed up owing to physical factors such as the disintegration of caseous masses. Although streptomycin seems to have a bactericidal effect on a rapidly growing culture at approximately the same level as it is bacteriostatic, it does not appear to be bactericidal to bacilli suspended in a non-nutrient medium (Middlebrook and Yegian, 1946; Garrod, 1948).

There is another factor of possible importance in the development of streptomycin-resistant strains and the assessment of their clinical significance. It may be that streptomycin-sensitive tubercle bacilli have, in the absence of streptomycin treatment, an advantage over the resistant strains as a result either of innate biological superiority or of weight of numbers. Karlson, Feldman, and Hinshaw (1947) found that guinea-pigs infected with strains of streptomycin-resistant tubercle bacilli survived longer than those infected with similar doses of sensitive organisms. This appears to be the only published evidence suggesting the lesser virulence of streptomycin-resistant strains.

The correlations obtained from the data in this paper are consistent with either of the mechanisms postulated to explain the development of resistant strains or with the suggestion that both mechanisms might be involved. Thus, if the development of resistance depends on a selective increase of a small number of resistant strains, within a milieu where streptomycin was active the larger, streptomycin-sensitive section of the patient's population of tubercle bacilli would be attacked both by the patient's own defences and by the streptomycin. The resistant organisms, on the other hand, would be affected by the patient's defences alone. This differential effect might account both for the late development of resistance in cases doing well initially and, if highly resistant strains were rarer than moderately resistant, for the high degree of resistance found in organisms from patients with poor initial response. Alternatively, it may be that the clinical condition is affected, even in the early stages of treatment, by a proportion of resistant organisms as yet insufficient to show in our test.

If, on the other hand, the development of streptomycin-resistant strains is facilitated by gradients of antibiotic activity within the lungs, it may be that the lesions present in those of our patients who showed a poor initial response favour the rapid production of resistant organisms; our results suggest a possible correlation between the initial degree of cavitation and the time at which resistant strains appeared. The same physical conditions might also favour the evolution of highly resistant organisms, though here we have not been able to demonstrate a correlation.

From this discussion it is plain that at present we can only make tentative suggestions about the mechanism by which streptomycin-resistant strains of tubercle bacilli appear in the sputum of cases of pulmonary tuberculosis under treatment with streptomycin. The problem is perhaps best summarized in the form of questions which still await a definite answer:

1. Are there gradients of streptomycin concentration or antibiotic activity within the lung? If so, do these favour the development of resistant strains?

2. Is there in the tuberculous patient a competition for survival between sensitive and insensitive organisms? In the absence of streptomycin treatment have the sensitive strains any advantage?

3. Do the sensitive bacilli isolated from the sputum in the early stages of a course of streptomycin represent a population actively increasing? If growth has ceased, do the viable bacilli in the sputum represent dormant organisms coughed up owing to physical factors such as the disintegration of caseous masses? What proportion of bacilli seen in a sputum smear are actually viable at different phases of treatment?

4. What is the proportion of resistant tubercle bacilli in the sputum when resistance shows in our tests? What is the proportion of bacilli resistant at the end of treatment, and does this correlate with clinical progress?

5. What is the distribution curve of resistance in the pre-treatment population of tubercle bacilli? Does this vary from case to case, and how does it change during the course of treatment?

The clinical significance of the development of resistance is still uncertain. In only two of our cases was there a clear change for the worse coinciding with the isolation of resistant organisms, whereas resistant strains were obtained from three cases in which cultures subsequently became negative. Other cases continued to improve in spite of the isolation of streptomycin-resistant organisms. In the main M.R.C. series, of which our cases formed a part, a considerable proportion of the treated cases continued to improve after the second month, the mean date of emergence of resistance being the 53rd day. This continued improvement might be due to the streptomycin continuing to act on a residuum of sensitive organisms or to the patient's defences taking over when the streptomycin ceased to be effective.

Summary

Increased resistance to streptomycin was observed in strains of tubercle bacilli isolated from 12 out of 13 cases of severe bilateral pulmonary tuberculosis treated with 2 g. of streptomycin a day for four months or more.

The rise in resistance varied from 4 to over 4,000 times that of the control strain H37Rv. Resistant strains were isolated from the 42nd day of treatment onwards. In the individual case resistance usually rose fairly rapidly to a plateau and then remained at about the same level.

When bacilli persisted in the sputum the numbers at first fell but after resistance had developed tended to rise again.

Streptomycin-resistant strains were isolated from three cases which subsequently became sputum-negative.

The time at which resistance developed and the degree of resistance attained were related to clinical progress before, but not after, resistant strains had been found. In cases which did poorly at first resistant strains were usually isolated early and attained a higher degree of resistance.

The higher the degree of resistance the more rapidly did it appear.

Only two cases showed any great change in clinical course coinciding with the time when resistant strains were first found.

The bearing of these results on the problem of the mechanism of development of streptomycin resistance and its clinical significance is discussed.

We are grateful for the co-operation of the physicians of the Brompton Hospital under whom these patients were admitted, and would like to thank the nursing staff of the hospital for cheerfully sustaining the added burden of work. Dr. J. W. Clegg, pathologist at the Brompton Hospital, has given us much help and encouragement, and Miss R. Weitz has done some of the laboratory investigations. This work was assisted by a grant from the Medical Research Council.

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STREPTOMYCIN IN GONORRHOEA

WITH ITS EFFECTS UPON DARK-FIELD POSITIVE LESIONS OF SYPHILIS

BY

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In the field of venereology streptomycin has great potentialities which have yet to be adequately explored. It apparently has some action against syphilis, but venereologists hope that this will prove slight, for streptomycin will then assume many of the present indications for sulphonamides in the treatment of venereal diseases in which syphilis is suspect but not proved (Willcox, 1948). Moore (1947) considers that the drug is unlikely to be clinically useful in syphilis, and points to the work of Dunham and Rake (1946), who found that the antisyphilitic effect of penicillin G was 3,000 times greater than that of streptomycin, though Herrell and Nichols (1945) treated four cases of early syphilis with doses of 1.2–10 g. of streptomycin and obtained a temporary absence of treponemata from the dark-field. Herrell (1947) later believed these results to be inconclusive and considered that so far there was no indication that the drug should be used in the treatment of this disease. Fisken and Gruhzit (1946) gave rabbits 1,000–3,000 subtilis units of streptomycin in three divided doses daily for 13–20 days and found no evidence whatever of any antispirochaetal action.

These observations are of considerable interest, for all reports indicate that streptomycin is particularly effective against gonorrhoea. This disease is at present being well controlled by penicillin and there is no clinical evidence of the development of penicillin resistance by the gonococcus on any substantial scale: many of the suspected cases so far reported have proved on investigation to be due not to the gonococcus itself but to a simultaneously acquired non-specific urethritis (Parkhurst *et al.*, 1947). The possibility that penicillin treatment of gonorrhoea might modify or mask an incubating syphilitic infection has been prominent in the minds of clinicians for some years, and indeed has been responsible for prolonging the period of

surveillance after treatment of gonorrhoea in this country. Such delayed syphilis is not often seen. This matter has been well discussed by Leeming (1947), though Cronin (1947) found little evidence to support this concept.

However, even though the masking of syphilis by penicillin should prove only a minor problem, if streptomycin will cure gonorrhoea in a single dose and at the same time leave the dark-field positive lesions of syphilis untouched it will still have a very definite place in the treatment of gonorrhoea. Especially will this be so in those cases with undiagnosed genital lesions or suspected false positive blood tests, in those persons with gonorrhoea who are known to have had recent intercourse with a syphilitic person, in the re-treatment of relapsing patients who showed Herxheimer-like reactions after the first treatment with penicillin, and in fact in all cases of gonorrhoea in which the risk of existing but undiagnosed concomitant syphilis is greater than the average. It may also be of value in cases in which it is desired that the period of subsequent surveillance should not exceed three months.

Streptomycin is effective against chancroid both in the experimental (Mortara and Saito, 1947) and in the human infection (Hirsh and Taggart, 1948a). In addition, most striking cures have been obtained in granuloma inguinale (Greenblatt *et al.*, 1947a, 1947b; Kupperman *et al.*, 1948; Marshak and Rodriquez, 1948; Hirsh and Taggart, 1948b; Barton *et al.*, 1947; Zimmerman and Smith, 1948). First reports of its action on non-specific urethritis are hopeful but equivocal (Pulaski, 1947; Kane and Foley, 1947), and my own experience will be the subject of a further paper. The drug has also been widely used in the treatment of urinary infections by Wilson (1948), Schwarz and Lazarus (1947), Keefer *et al.* (1946b), and Finland *et al.* (1946) with upwards of 50% success. In all cases failure seems to be due to a resistance which is very rapidly acquired; but better results, both experimentally and clinically, are obtained in an alkaline medium (Knop, 1946; Kane and Foley, 1947).

Resistance to streptomycin, once acquired, seems to be permanent. Murray *et al.* (1947) found that it continued through more than 100 transfers in a streptomycin-free broth, and Miller and Bohnhoff (1947) noted that two or three transfers in media containing increasing concentrations of streptomycin sufficed to permit the meningococcus to grow in a concentration of 50,000 μg. of streptomycin per ml., whereas no fewer than 147 such subcultures were required for the same organism to grow in a concentration of only 5,000 units per ml. of penicillin.

One injection of streptomycin may cure gonorrhoea, and provided the dose is adequate the question of resistance does not arise, though streptomycin-resistant strains of the gonococcus may well appear in the same way as with the sulphonamides. Chinn *et al.* (1947) had all of 25 cases of gonorrhoea cured by a single injection of 0.5 g. of streptomycin, all of 10 with 0.4 g., and 15 others with 0.3 g. Though three out of five failed with doses of 0.1 g. there were only two failures out of 22 treated with single injections of 0.2 g., and toxic reactions were negligible throughout. It is noteworthy that two of these patients developed Herxheimer-like reactions at the time of treatment, and both were later shown to have syphilis. Pulaski (1947) treated nine cases of apparently penicillin-resistant gonorrhoea, and had complete success in seven. The two failures were improved clinically, but the complications of prostatitis and epididymitis were not resolved.

After a single injection of 0.5 g. of streptomycin the peak level in the blood is reached within an hour (Molitor, 1947), and effective levels are still present at eight hours. For continued administration Loewe and Alture-Werber (1947) consider that six-hourly injections should suffice. The drug is excreted in the bile and urine, and may be recovered from the latter (Lamensans *et al.*, 1947).

The toxic effects of streptomycin include histamine-like reactions, headache, flushing of the skin, neurological disturbance, vertigo, paraesthesiae, and hypersensitive skin reactions; and there may be an eosinophilia (Keefer *et al.*, 1946a). There may also be renal impairment with cylindruria, which is possibly prevented by alkalis. These reactions are not usual after single injections of the drug, and, even with more prolonged administration, McDermott (1947) considers 3 g. the maximum safe daily dose. Skin sensitization, developing in a few months in those handling the drug, has also been reported (Strauss and Warring, 1947).

Streptomycin is given intramuscularly in aqueous solution. Preliminary tests have shown no advantages in a peanut-oil–beeswax suspension as with penicillin (Kolmer *et al.*, 1946); neither is the action of the drug satisfactory if it is administered orally. However, up to 0.1 g. in aqueous solution has been successfully given by the hypospray (jet injection) (Hirsch *et al.*, 1948).

Case Histories

The following case records confirm the claim that a single dose of streptomycin in aqueous solution is capable of curing gonorrhoea as effectively as penicillin—possibly more effectively—and that the same dose will not adversely influence the dark-field positive lesions of syphilis.

Syphilis

Case A.—The patient, a white man aged 23, had a typical penile chancre of two weeks' duration. Characteristic left inguinal adenitis was also present, and the Wassermann and Kahn reactions of the blood were strongly positive. The first dark-field examination was disappointingly negative, but two days later *Treponema pallidum* was visualized without difficulty. He was then given a single intramuscular injection of 0.6 g. of streptomycin in 6 ml. of isotonic saline; 24 hours later the sore had not altered in appearance and the responsible organism was still readily recoverable.

Case 1. Acute Gonorrhoea in the Male

A white man aged 27, the husband of Case 2, was first seen on Sept. 11, 1948, with a purulent urethral discharge of three days' duration. Gonococci were observed in the smear and the urine was hazy only in the first glass. He denied other than marital intercourse, which last took place four days previously. The only treatment given was a single intramuscular injection of 0.6 g. of streptomycin in 2 ml. of normal saline. Two days later the discharge had vanished, smears and cultures from the urethra were negative for the gonococcus, and the urine was quite clear. No gross upset was noted from the injection, though he did comment that when driving his car home from the clinic after the injection he had experienced an odd sensation as if objects were flying past at an abnormal speed.

The following day, however, the discharge recurred, though he denied further exposure or the taking of alcohol. His wife (Case 2) was also infected, and both consistently denied any extramarital relations, but the possibility of reinfection cannot be entirely excluded. A week after the first visit the discharge was as profuse as before and gonococci were once again present in the smear. A second dose of 0.6 g. of streptomycin (this time in 6 ml. of normal saline) was given intramuscularly. No untoward disturbance was noted on this occasion, apart from a transient headache four hours afterwards. The discharge again disappeared within 24 hours. At 48 hours the urine had completely cleared and gonococci were not obtained in urethral smear or culture.

A week after the second injection the findings were still negative and no abnormalities were detectable in the prostatic

bead or prostatic culture. Two days later he was allowed alcohol and protected intercourse with his wife (Case 2), who had also been treated with streptomycin. Actually, unprotected intercourse began the following night, but one, three, and eight weeks later no ill effects were reported by either partner.

Case 2. Acute Gonorrhoea in the Female

A white woman aged 27, the wife of Case 1, denied other than marital intercourse, which last took place six days previous to her attendance as a contact, she being quite symptom-free. On examination, however, a pronounced urethritis and a cervicitis were found, though erosion was not present. Smears of the discharges showed gonococci in both the cervix and the urethra. She was given a single intramuscular injection of 0.6 g. of streptomycin in 2 ml. of isotonic saline. Two days later no visible discharge was apparent in either cervix or urethra and, though some pus was still evident microscopically in smears from both sites, no gonococci were observed and none were found on culture.

The patient reported that she had slight pain at the injection site on the day of the injection, and that she had experienced symptoms of influenza two days later. Serum tests for syphilis, however, remained negative in both husband and wife. One week and two weeks later the urethral and cervical smears and cultures were completely free from pus and gonococci, and, as a test of cure for both partners, protected intercourse with her husband was urged. In actual fact unprotected intercourse took place the following night, and this was succeeded immediately by a menstrual period. When seen at the conclusion of this, three weeks after treatment, and again one and six weeks later, the smears and cultures from both urethra and cervix were still negative.

Case 3. Penicillin Relapse

This patient, a white man aged 28, was first seen on Sept. 6, 1948, when he presented an acute gonococcal urethritis of two days' duration which was treated with a single intramuscular injection of 300,000 units of penicillin in oil–beeswax. Five days later there was no discharge and the urine was clear, but on Sept. 20 the discharge, which contained an abundance of gonococci, was again profuse, having relapsed four days previously. No history of fresh exposure or alcoholic excess was admitted. He was then given a single intramuscular injection of 0.2 g. of streptomycin in 2 ml. of normal saline and the discharge disappeared within 24 hours. Nine days later he continued well, the urine was entirely clear, and no gonococci were found in urethral or prostatic smears and cultures. Further prostatic smears and cultures taken two weeks after treatment were also negative.

Case 4. Gonorrhoea of Long Standing

The patient, a white man aged 23, developed an acute urethral discharge on July 8, 1948, and gonococci were isolated in the smear. Surprisingly, he left for the Continent the next day without receiving any treatment, and remained untreated until Sept. 24, when the discharge was as profuse as ever and many gonococci could be seen in the smear. No complications had developed. He then received a single intramuscular injection of 0.3 g. of streptomycin in 3 ml. of normal saline. Two days later there was no discharge, and the urine, previously hazy, was now quite clear. The urethral smear showed a trace of pus but no gonococci, and the culture was also negative. Eight days later prostatic smears and cultures gave entirely satisfactory results. He then moved elsewhere, but seven weeks after treatment wrote saying he was well.

Case 5. Gonorrhoea: Sulphonamide Relapse

This patient, a white man aged 23, was first seen on July 17, 1948, having received 36 g. of sulphapyridine over 12 days from his own doctor for a urethral discharge the aetiology of which was never determined. Apart from some dampness of the urethra there was no discharge and the urine was clear. No treatment was advised, but he was kept under observation until Aug. 28, when he was still symptom-free, the urine being clear and the prostatic secretion free from pus. On Sept. 27 he attended with a slight mucopurulent discharge of one day's duration. He denied fresh contact, yet gonococci were observed in the smear. The urine was still clear, but there were many threads in the first glass. He received a single intramuscular injection of 0.4 g. of streptomycin in 4 ml. of normal saline. One, two, and seven weeks later there was no discharge and the urine was clear and free from threads; urethral and prostatic smears and cultures were also entirely negative.

Case 6. Complicated Gonorrhoea: Cowperitis

A negro man aged 30 was successfully treated for gonorrhoea in 1945, in August, 1947, and in September, 1947, when he was given 200,000 units of penicillin. On the last-mentioned occasion he relapsed two days later, developing an abscess of the left Cowper's gland which ruptured exteriorly. On July 29, 1948, he again developed an acute gonorrhoea, which was successfully treated with a single injection of 300,000 units of penicillin in oil–beeswax; but five days later the left Cowper's gland was palpable as a small tender nodule and he was given a course of sulphadiazine in addition.

He defaulted from observation, but returned on Sept. 29 with yet another apparently fresh attack of gonorrhoea. Gonococci were present in the smear, and the urine was grossly hazy with threads. The left Cowper's gland was just palpable and was acutely tender. It was decided to treat him with streptomycin, though the very small dose of 0.2 g. in 2 ml. of normal saline was the only amount available. This was given intramuscularly, and when seen 24 hours later the discharge had gone though there was still some urethral dampness, a smear of which showed a moderate amount of pus cells but no gonococci. The urethral culture was also negative, the urine was clear and contained a few threads in the first glass only, and a rectal examination revealed no perineal tenderness.

Though the initial success of even this small dose was truly spectacular, not surprisingly it proved insufficient, for two days later the discharge again recurred, and when he attended a week after treatment there was a gross urethral discharge with gonococci present in the smear and a fluctuant left perineal abscess the size of an olive. This was aspirated, some 3 ml. of yellow pus being removed, and he was then given eight daily injections of 600,000 units of penicillin in oil–beeswax. Improvement was immediate, steady, and complete, and has been maintained.

Case 7. Uncomplicated Gonorrhoea

This patient, a white man aged 43, had a profuse urethral discharge of three days' duration when first seen. Gonococci were present in the smear, and the urine was hazy only in the first glass. Twenty-four hours after a single injection of 0.2 g. of streptomycin in 2 ml. of normal saline the urethral discharge had entirely disappeared. At 48 hours only epithelial cells were recoverable from the smear, and the urethral culture was also negative. The urine, too, was quite clear and free from threads. After one, two, and five weeks his condition continued to be satisfactory; the prostatic bead was free from pus and no gonococci were obtained in smear or culture.

The gonorrhoea cases, none of which showed any clinical or serological evidence of syphilis, are summarized in the following Table.

No.	Type	Sex	Dose	Initial Result	Later Events	Final Result
1	Simple	M	0·6 g.	Success	Recurrence after 3 days; re-treated with streptomycin	Success 56 days
2	„	F	0·6 g.	„	—	Success 63 days
3	Penicillin relapse	M	0·2 g.	„	—	Success 14 days
4	Protracted gonorrhoea	M	0·3 g.	„	—	Success 49 days
5	Sulphonamide relapse	M	0·4 g.	„	—	Success 49 days
6	Complicated Cowperitis	M	0·2 g.	„	Relapsed after 2 days; re-treated with penicillin	—
7	Simple	M	0·2 g.	„	—	Success 35 days

Summary

Seven cases of gonorrhoea (six males and one female), of which six were uncomplicated and one was complicated by Cowperitis, have been treated with single intramuscular injections of 0.2–0.6 g. of streptomycin in an aqueous medium. In all cases the initial response was at least as dramatic as treatment with penicillin in watery or oil–wax media. One patient, given 0.6 g., apparently relapsed after three days, but was successfully re-treated with the same dose of the drug. Another, complicated by Cowperitis, received only 0.2 g., and after a satisfactory initial response relapsed two days later with abscess formation in the gland and was then treated successfully with penicillin.

One patient with dark-field positive primary syphilis was given a single intramuscular injection of 0.6 g. of streptomycin, and twenty-four hours later *T. pallidum* was still recoverable without difficulty from the dark-field.

Apart from possible mild cerebral effects in Case 1, and mild pain at the site of injection in Case 2, no toxic effects were recorded.

It is concluded that streptomycin will be of the greatest value in venereology for all cases of gonorrhoea in which syphilis is more than usually suspect. As it appears that its use may not mask an incubating syphilitic infection, it is probable that only a three-months post-treatment period of surveillance to exclude syphilis will prove necessary for gonorrhoea treated with streptomycin, as compared with the six months usual after treatment with penicillin.

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LARYNGEAL PARALYSIS ASSOCIATED WITH CARDIAC HYPERTROPHY

REPORT OF FOUR CASES

BY

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The association of laryngeal paralysis with aneurysm of the aortic arch is well known. That the left recurrent laryngeal nerve may be damaged in cases of cardiac enlargement is, however, less well recognized. The paralysis usually occurs in association with mitral stenosis, but recently some instances have been recorded of vocal-cord palsy in cases of hypertension with cardiac failure. The present communication is based on four cases of laryngeal paralysis attributable to a coexisting cardiac lesion.

Case Reports

Case 1.—A woman aged 26 was examined in consultation with Dr. James Richard on account of huskiness of a few months' duration. Laryngoscopy revealed complete abductor paralysis of the left vocal cord. The physical signs in the chest were those of cardiac enlargement and mitral stenosis with incompetence. The apex beat was 4 in. (10 cm.) from the midline, and the right border of dullness was at the right border of the sternum. There was slight oedema of the ankles. Her compensation was fairly good for a quiet life but failed on any exertion. Since the age of 19 she had been troubled with dyspnoea on exertion, palpitations, and oedema of the ankles. At the age of 7 she had had chorea followed by subacute rheumatism, at 10 peliosis rheumatica, at 14 tonsillitis, and at 19 subacute rheumatism.

Case 2.—A woman aged 51 was admitted to Dr. George Allan's wards in the Western Infirmary complaining of breathlessness and insomnia for three weeks and also of pain in the left leg and foot. During the previous two years her health had been poor—she was easily fatigued and had slight breathlessness. There was no history of rheumatism or other major illness. The lips and cheeks were cyanosed and there was considerable dyspnoea, which was increased even by speaking. The voice was hoarse. Both ankles were oedematous, the left one being tense and tender. The cardiac rhythm was regular at 150 and the pulse was of poor volume and tension. The blood pressure was 135/100. The arteries were not palpable. The apex beat was diffuse and visible and most forcible to palpation in the sixth interspace at 5¼ in. (13.3 cm.) from the mid-sternal line. The borders of cardiac dullness were at the third rib, the mid-sternal line, and 5¼ in. from the mid-sternal line. A loud musical murmur replaced the first cardiac sound and was conducted all over the praecordium and into the axilla. The second pulmonic sound was markedly accentuated. Laryngoscopy revealed complete paralysis of the left vocal cord. Examination of the fundi revealed slight arteriosclerotic changes. The patient died three weeks after admission. Permission for necropsy was not obtained.

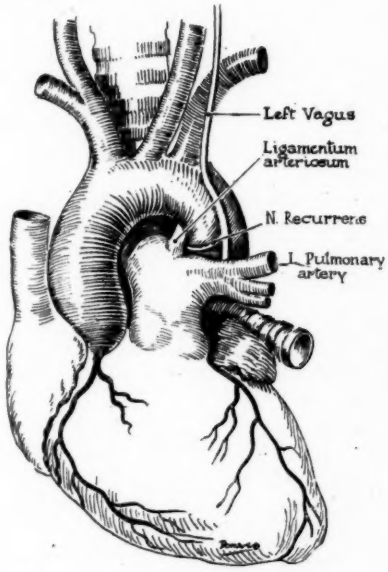
Case 3.—A married woman aged 53 was admitted on May 19, 1933, to the Western Infirmary suffering from severe abdominal and left thoracic pain, tachycardia, and slight jaundice. She had had cholecystectomy for gall-stones in June, 1932, but had had recurrent attacks of jaundice during the following winter. The tachycardia was ascribed to auricular flutter, which with digitalis changed to auricular fibrillation and ultimately to regular rhythm. There was no material improvement, pain persisted, and she succumbed to hypostatic pneumonia on July 9. Paralysis of the left vocal cord was observed on laryngoscopy on June 27. The necropsy findings were as follows. The heart weighed 12 oz. (340 g.). The pericardium was healthy and the left ventricle was of normal size. The left auricle was markedly dilated, as were to a lesser extent both chambers of the right heart. The mitral valve was stenosed, being 7/10 in. (1.78 cm.) in diameter. The tricuspid

and arterial valves were healthy and of normal dimensions. The myocardium was somewhat fibrosed. The divided ends of the large vessels were tied off and the heart filled with water. It was noted that the left auricle did not actually impinge on the left recurrent laryngeal nerve, which showed a constriction at the point where, having left the vagus, it passed between the left pulmonary artery and the arch of the aorta. The nerve at the affected point was flattened and much attenuated.

Case 4.—A man aged 34 was seen in consultation with Dr. R. G. Lendrum at the medical dispensary of the Western Infirmary. Five weeks previously his voice had become suddenly weak, and there had been some precordial pain. There was considerable cardiac enlargement, with signs of mitral stenosis, but no dyspnoea or oedema. The patient had had several attacks of rheumatic fever. Laryngoscopy showed paralysis of the left vocal cord.

Discussion

Before discussing the mechanism of production of the paralysis, the relations of the structures involved require consideration. The left recurrent laryngeal nerve arises from the vagus to the left of the aortic arch on a level with its lower border. The nerve winds below the arch immediately behind the attachment of the ligamentum arteriosum to the concavity of the arch, and ascends to the side of the trachea. The ligamentum arteriosum, the fibrous cord which remains from the closure of the foetal ductus arteriosus, extends from the upper aspect of the root of the left pulmonary artery to the aorta. The relations of the left auricle, pulmonary artery, and aortic arch are shown in the accompanying diagram.



Ortner (1897) advanced the theory that distension of the left auricle produced paralysis by direct pressure on the nerve, and considered that it was supported by the evidence of necropsy in his two cases. Enormous dilatation of the left auricle was found, great enough to produce pressure on the aortic arch and to squeeze the recurrent nerve where it wound beneath the arch. The nerve was completely flattened and atrophied.

Kraus (1900) encountered a necropsy where this theory appeared to be inapplicable. The heart was well compensated, and dilatation of the auricle was insufficient to exert direct pressure on the nerve. He suggested the following explanation. In a well-compensated mitral lesion in which considerable hypertrophy of cardiac musculature has taken place the heart comes to lie more horizontally with its right border on the diaphragm. In such a case the normal "bascule" or seesaw action is exaggerated. It is thought that, during systole, traction on the pulmonary artery is forcible enough to pull on the aortic arch through the medium of the ligamentum arteriosum, thereby stretching the recurrent nerve.

Fetterolf and Norris (1911), however, have thrown doubt on the probability of that explanation. They point out that the ligamentum arteriosum runs more or less horizontally, that the arch is supported at both ends, and that it is slung up by its attachment to the cervical fascia. They maintain from their studies of formalin-hardened sections of the thorax that dilatation of the auricle acts indirectly by forcing upwards and backwards the pulmonary artery, which itself is often dilated.

King, Hitzig, and Fishberg (1934) reported three cases of hypertension and arteriosclerotic heart disease with failure of the left ventricle. Coronary thrombosis had occurred in two of the cases, and in all three the left recurrent nerve had been paralysed. They regard the dilatation of the pulmonary artery produced by the engorgement of the lesser circulation as the cause of the compression of the nerve against the arch of the aorta and the ligamentum arteriosum. They conclude that the hypertension in the lesser circulation is an important factor in the production of laryngeal paralysis complicating mitral lesions. The evidence available at necropsy in one of our cases lends support to this explanation, which appears to be the most probable one. Hypertension in the pulmonary artery is a constant feature in mitral lesions before failure of the lesser circulation has occurred, whereas, according to the findings in the limited number of necropsies which have been performed in these cases, the relation of the dilated left auricle or its appendage to the recurrent nerve is very variable.

To judge from the literature, the syndrome is infrequently encountered, and it is to be noted that many of the recorded cases have not been substantiated by necropsy. Since attention was first drawn to it by Ortner in 1897 about 80 cases have been recorded. Osler (1905), however, had seen only two instances and referred to the possibility of confusing aortic aneurysm with mitral stenosis when vocal-cord paralysis also exists. In the systematic examination of 20 cases of mitral disease Ceraulo (1907) found the left vocal cord paralysed in four. Garland and White (1920) reported nine cases collected from the records of the Massachusetts General Hospital during a period of eight years. In a series of 50 cases of advanced cardiac disease with hypertrophy we encountered two with associated laryngeal palsy (Cases 2 and 3), and it therefore seems probable that the condition occurs more often than is suggested by the scarcity of recorded cases.

I wish to acknowledge my indebtedness to my medical colleagues for clinical notes and for the opportunity of examining cases in their wards.

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Occupation centres provide for mentally defective children unable to attend school because they are incapable of receiving education there. Local authorities have recently been asked to submit plans for the training of defectives at home and in the centres, and the National Association for Mental Health has recently published an interesting survey entitled "Occupation Centres for Mentally Defective Children" which may serve as a guide to the problem. Detailed information, as well as the pamphlet (price 9d.), may be obtained from the National Association at Maurice Craig House, 39, Queen Anne Street, London, W.1.

PURPURA HAEMORRHAGICA AS A COMPLICATION OF PREGNANCY

BY

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Purpura haemorrhagica is generally regarded as a rare but very grave complication of pregnancy. Patterson (1946) collected from the literature reports of 62 cases from 1867 up to the date of his paper. To these he added a further case. He found the maternal mortality was 55%. Mosher (1923) also studied the recorded cases and believed the maternal mortality to be almost 100%, the commonest cause of death being post-partum uterine bleeding. He described the common association of purpura with premature delivery at the sixth to seventh month and noted that infection was usually superimposed. The foetal mortality in his series was in the region of 50%. Rushmore (1925) collected a series in which the maternal mortality was 58% and the foetal mortality 64%. He quoted as typical the case described by Puech in which premature labour occurred at the sixth month and death on the second day of the puerperium from exsanguination as a result of prolonged and persistent uterine bleeding following delivery.

Clinical Picture

In most of the cases in Patterson's series there was no evidence of purpura before the pregnancy, but haemorrhages into the skin and mucous membranes developed at various times during the course of the pregnancy. In addition epistaxis, haemoptysis, or haematuria may be present. The platelet count is lowered and the bleeding time prolonged. Anaemia is usually present, and there may be a personal and a family history of bleeding, as in Patterson's case. This patient's great-grandmother and grandmother were known to have been bleeders, and her mother, when she herself was born, suffered from post-partum haemorrhage and required transfusion. The patient herself had had symptoms of purpura from the age of 4 and in spite of advice to the contrary had become pregnant. Hess's tourniquet test may be positive. The spleen may or may not be enlarged, and Polowe (1944) described a case of splenoma in which extensive areas of necrosis were present in the spleen.

Pregnancy usually continues uneventfully, and labour may be normal until the third stage is completed, when difficulty may be found in controlling the continuous haemorrhage which tends to occur from the uterus and which may lead to death after some days or perhaps hours. Haemorrhage may take place not only from the uterus but also from lacerations of the cervix, vagina, or parametrium, and haematomata may form deep to the vaginal wall as a result of trauma from the passage of the foetal head or from forceps application. When purpura is present pre-eclamptic toxaemia is particularly dangerous owing to the special risk of placental separation and massive intra-uterine haemorrhage. In this connexion Titus (1940) states that some fulminating types of placental separation may be due to purpura.

The bleeding time and platelet count may be normal, but acute attacks of purpura may occur during pregnancy if the platelet count is low. The infant is sometimes affected, but, according to Polowe (1944), more commonly it escapes. Siegler (1934), however, has recorded a case where the mother survived but the infant died of haemorrhage. Patterson distinguishes between chronic purpura, in which pregnancy is a risk so grave that it should not be undertaken, and acute purpura arising during the pregnancy. In the latter type of case, similar to the one described below, complete recovery may take place and the bleeding time and platelet count, together with the other blood findings, may return to normal before the onset of labour, with or without specific treatment.

Treatment

The treatment most generally advocated is the use of repeated small transfusions of about 200 ml. of fresh blood in an attempt to improve the blood's condition. Iron and calcium may sometimes be given with advantage. Vitamin K will often help to restore bleeding and clotting times to normal. Polowe, who quotes a successful case operated on in the eighth month of pregnancy, advocates splenectomy in all cases, but Patterson considers that this should be reserved for those cases in which conservative treatment fails or in which definite splenomegaly is found.

Interruption of the pregnancy during the acute stage is contraindicated, since this will merely open another channel for haemorrhage. Every effort should therefore be made to keep the pregnancy going until the acute stage is over and to improve the platelet count. Delivery should be carried out with as little interference as possible, since the trauma of an instrumental delivery may lead to extensive bleeding in the paravaginal tissues even in the absence of vaginal laceration. Episiotomy and perineal tears are a further possible source of bleeding and should be avoided.

Bleeding at delivery is not usually excessive, but it continues for hours or days afterwards. Patterson recommends that the uterus and vagina should be packed for 48 hours if there is any bleeding after completion of the third stage. At the end of 48 hours the pack should be removed, but it should be reinserted if bleeding recurs and again removed after a further 48 hours. In view of the danger of infection, treatment with penicillin or sulphonamides may be indicated. When bleeding cannot be controlled by other means hysterectomy may be necessary, but there are strong reasons for not operating on these patients if it can be avoided.

As the infant may be affected by the disease a platelet count should be done as soon as possible after birth, and the child should be observed carefully for evidence of haemorrhage. If necessary transfusion should be undertaken.

Prognosis

The very high mortality rate for both mother and foetus shows how serious is the outlook, but in cases of transient purpura complete recovery may take place before labour begins. A distinction should therefore be made between patients in whom the platelet count is low at the onset of labour and those in whom labour follows some time after all evidence of purpura has disappeared. The following case report shows that the condition may be mild and need not give rise to anxiety.

The patient, a doctor's wife aged 29 years, was first seen at the 35th week of her second pregnancy, the morning after the appearance of a purpuric eruption on the face, neck, and shoulders. Her first pregnancy had been normal in every respect, and her general health had always been good. There had never been any evidence of a tendency to bleeding. Menstruation was always normal and menstrual loss not excessive. During her pregnancy she had been well, and her diet had been adequate. The day before being seen by me she had vomited some undigested food in the evening, but no blood had been noticed in the vomited material. Following this a purpuric rash had been noted on the face, neck, and shoulders. The left forearm gave a positive response to Hess's test, her husband

having taken her blood pressure as soon as the purpuric rash appeared. There was no corresponding rash on the opposite forearm or any sign of bleeding elsewhere. The pregnancy appeared to be normal; the vertex was presenting and the head was still free. Blood pressure was 110/70, and no albuminuria was found.

The patient was brought into hospital, where she was seen in consultation with Professor Stanley Alstead, under whose supervision full blood investigation was carried out. The most significant finding here was a platelet count of 101,500 per c.mm.—i.e., about 40% of the accepted minimum standard. There were some red blood cells in the urine, singly and in small clumps, and clotting time was prolonged to 14 minutes. In a few days, however, without any specific treatment, the rash disappeared and no new ecchymoses were observed. The pregnancy seemed to be progressing normally. There was no evidence of toxaemia, so it was decided to await events. She was discharged from hospital and returned to her home.

A week before term full blood investigation was repeated and appeared to be normal in all respects. The platelet count was 562,320 per c.mm. and the clotting time 6 minutes 45 seconds. The foetal head was by this time engaged in the pelvis, and the pregnancy seemed to be normal. As a precautionary measure it was decided that she should have a small transfusion of fresh blood at the onset of labour and that vitamin K should be given at the same time. A week later there was a small "show," and a slow transfusion of 250 ml. of Group IV blood was given together with vitamin K ("kapilon," 4 ml.). A few hours after this labour began; it was completed in about three hours with the delivery of a live female child weighing 8 lb. Immediately after the birth of the shoulders ergometrine, 0.5 mg., was given intravenously and the placenta and membranes were delivered complete without any apparent haemorrhage. There were no lacerations and the uterus contracted well. After the completion of labour bleeding was normal in amount and gave rise to no anxiety. The puerperium was uneventful, and on the fifth day the platelet count was found to be 340,000, the other blood findings also being normal. The child made good progress, being fully breast-fed, and did not seem to be affected by purpura, its platelet count on the twelfth day being 346,000. Both mother and child were discharged home in good condition on the 14th day, and subsequent progress has been uneventful.

Discussion

In 63 previously reported cases of purpura haemorrhagica complicating pregnancy the mortality in both mother and foetus has been alarmingly high, the most recently recorded figure for the former being 55%. The commonest cause of death is prolonged haemorrhage after the completion of the third stage. The case quoted above was mild and transient. Special precautions were taken before and after labour; no undue haemorrhage was observed and the puerperium was normal in all respects. The infant was unaffected. This case confirms Patterson's opinion that there are two different types of case—namely, the chronic, which is associated with all the dangers giving rise to high mortality, and the acute, in which the abnormality may pass off before labour begins and there is no particular danger. The prognosis is good in the acute case unless the acute phase and the onset of labour should unfortunately coincide, but it is not possible to give a prognosis regarding recurrence in a subsequent pregnancy. In view of the very small number of cases recorded it is unlikely that recurrence is common.

Summary

Purpura haemorrhagica is a rare complication of pregnancy. The literature, in which there are records of 63 cases, has been reviewed. A further case is now added.

In the case recorded the purpura was acute and transient, and labour was unattended by any complication.

Treatment should be directed to restoring the blood picture to normal before the onset of labour. If this is impossible special measures for the control of post-partum haemorrhage may be necessary.

The prognosis in the acute cases is good, but there is grave danger of maternal death in the chronic cases.

The foetus is commonly involved, and may die of haemorrhage or of prematurity associated with the early onset of labour in a considerable proportion of these cases.

I am indebted to Dr. H. J. R. Kirkpatrick, Dr. Elemer Forrai, and Dr. Edgar Moyes for the blood investigations in this case, and to Professor Stanley Alstead for his advice in the management of it.

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POLIOMYELITIS

EFFECT OF EXERTION DURING THE PRE-PARALYTIC STAGE

BY

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A history of great physical exertion immediately preceding the onset of severe paralysis in attacks of poliomyelitis has often been recorded, but until recently no statistical evidence was available to determine whether such instances were more frequent than chance would dictate. Russell (1947) made a very careful statistical analysis of the degree of physical activity and resulting paralysis in 44 cases of poliomyelitis, and concluded: "Physical activity of any

TABLE I.—*Effect of Physical Activity during the Pre-Paralytic Stage on the Severity of Paralysis in 30 Cases of Poliomyelitis. P indicates onset of Paralysis*

No.	Age	Sex	Day After Onset of Pre-paralytic Symptoms							Paralysis on Admission	Residual Paralysis at 3 Months
			D+1	D+2	D+3	D+4	D+5	D+6	D+7		
1	8	M	Nil	Nil	2	2	P	—	—	C	B
2	33	F	,,	1	2	1	1	P	—	B	A
4	1 11/12	M	,,	1	1	1	P	—	—	B	B
5	7	F	,,	2	P	—	—	—	—	C	B
6	26	F	2	2	2	Nil	P	—	—	C	A
10	3	M	Nil	Nil	1	1	P	—	—	D	B
11	1½	M	2	2	Nil	Nil	P	—	—	C	B
13	4	F	1	P	—	—	—	—	—	C	C
15	23	F	Nil	3	3	P	—	—	—	C	F
16	7	F	1	1	P	—	—	—	—	F	B
17	5	F	1	1	2	2	2	—	P	C	B
18	34	F	Nil	Nil	Nil	P	—	—	—	D	C
19	3	F	,,	,,	P	—	—	—	—	B	A
20	12	M	,,	,,	Nil	Nil	Nil	P	—	E	D
21	17	M	2	P	—	—	—	—	—	F	F
22	2	M	Nil	Nil	Nil	Nil	Nil	P	—	B	A
23	17	M	,,	,,	P	—	—	—	—	E	E
25	1	F	,,	,,	P	—	—	—	—	B	A
26	1½	M	1	1	P	—	—	—	—	B	A
27	14	F	1	2	Nil	Nil	P	—	—	B	B
28	9	M	Nil	Nil	,,	,,	P	—	—	B	A
31	28	F	1	1	,,	,,	Nil	P	—	E	C
32	5	F	Nil	Nil	P	—	—	—	—	C	B
35	5	F	,,	,,	P	—	—	—	—	B	A
36	34	F	,,	,,	Nil	P	—	—	—	B	A
37	35	M	3	3	1	1	Nil	P	—	F	F
38	22	M	2	2	3	P	—	—	—	C	C
40	30	F	1	Nil	P	—	—	—	—	F	F
41	35	M	3	2	P	—	—	—	—	C	F
42	21	M	3	3	1	Nil	P	—	—	F	F

Degree of physical activity.—Nil = in bed. 1 = not more than ½ day light work (e.g., resting in house, with short walks). 2 = Average light work (e.g., secretarial, housework, school). 3 = Average or heavy manual work (e.g., factory, labourer, athletic sports).

Severity of paralysis.—A = No paralysis. B = No severe paralysis, probable recovery to full function. C = Moderate paralysis—i.e., moderate multiple paralysis or severe paralysis of a few muscles in one limb. D = Bilateral severe paralysis at any level including trunk, or gross paralysis of one limb. E = Severe and extensive paralysis such as trunk and both lower limbs, or severe paralysis of all limbs. F = Fatal.

kind during the pre-paralytic stage increases the danger of severe paralysis. Complete physical rest in bed during the whole of the pre-paralytic stage seems to protect the patient from severe paralysis."

A similar analysis of cases of poliomyelitis occurring in Cornwall during 1947–8 is shown in Table I. The cases are selected in so far that only those giving a clear history of a pre-paralytic meningeal stage of the illness are included. The standards adopted for the criteria of meningeal involvement, the severity of physical activity, and the degree of paralysis are the same as used by Russell, differing only in that the degree of paralysis in my cases is estimated after three months' treatment instead of on admission. Two of the cases (Nos. 34 and 38) had travelled to Cornwall by road during the pre-paralytic stage of the illness. In both cases the patient had personally driven his car 250 miles or more.

TABLE II.—*Showing Maximum Physical Activity in any one Day following First Meningeal Symptoms and Severity of Paralysis*

Paralysis at 3 Months	No. of Cases	Physical Activity, Showing Maximum Activity in 24 Hours			
		Nil (Bed)	1 Slight	2 Moderate	3 Severe
None (A) ..	9	6	1	2	—
Slight (B) ..	9	1	3	5	—
Moderate (C) ..	4	1	3	—	—
Severe (D) ..	1	1	—	—	—
Very severe (E) ..	1	1	—	—	—
Death (F) ..	6	—	—	1	5

Table II shows the maximum activity in a single day and the severity of the resultant paralysis. It will be noted that patients who took to their beds with the onset of initial symptoms proved to be relatively mild cases, six of the ten cases having no residual paralysis after three months of treatment, whereas severe activity in the pre-paralytic stage of the disease led to a very grave prognosis: five of the six fatal cases had undertaken severe mental or physical strain in the days immediately before the onset of paralysis.

TABLE III.—*Showing Aggregate Physical Activity in Pre-paralytic Stage and Severity of Paralysis*

Paralysis at 3 Months	No. of Cases	Physical Activity—Total Incidence								
		0	1	2	3	4	5	6	7	8
None (A)	9	6	1	—	—	—	1	1	—	—
Slight (B)	9	1	—	3	2	2	—	—	—	1
Moderate (C)	4	1	2	1	—	—	—	—	—	—
Severe (D)	1	1	—	—	—	—	—	—	—	—
Very severe (E)	1	1	—	—	—	—	—	—	—	—
Death (F)	6	—	—	1	—	—	1	1	3	—

Table III shows the degree of paralysis plotted against the aggregate of physical activity during the pre-paralytic period. It will be seen that the maximum exertion in any one day is a more important indication of the prognosis than the aggregate of physical activity during the period.

Summary

The effect of physical or mental exertion during the pre-paralytic stage of poliomyelitis on the ultimate prognosis is analysed in thirty cases of the disease which occurred in Cornwall during 1947–8.

The findings support those of Russell (1947)—namely, that severe physical activity during the pre-paralytic stage is associated with grave prognosis. Severe mental strain, such as driving a car over long distances, appears to be equally disastrous, whereas paralysis tends to be mild in cases confined to bed during the pre-paralytic stage.

I wish to thank Dr. J. G. M. Molony for granting me facilities to examine these cases during their stay in the County Isolation Hospital.

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Medical Memoranda

A Case of Tetanus Treated with *d*-Tubocurarine Chloride

The use of curare in tetanus was described by Hunter (1878) and later by Hale-White (1901). More recently Florey, Harding, and Fildes (1934), Cole (1934), Mitchell (1935), West (1936), Isacson and Swenson (1941), and Cullen and Quinn (1943), using various preparations of curare, were of the opinion that beneficial effects were produced by the use of the drug in this disease. It is felt that the following case history may be of interest now that a derivative of curare (*d*-tubocurarine chloride) is readily available.

CASE HISTORY

A lad aged 16 was admitted on April 23, 1948. Pain and stiffness in the lumbar muscles and jaw had started 36 hours previously. Owing to repeated injuries at football the incubation period of the disease is uncertain. On admission his temperature was 97.2° F. (36.2° C.), pulse 90, and respiration rate 24. His general condition was good and he weighed 8 stone (50.8 kg.). On his right shin there was a scabbed sore ¾ in. (1.9 cm.) in diameter, together with a few scratches. Risus sardonicus and trismus were present, and he was unable to separate his incisor teeth more than half an inch (1.25 cm.). There was marked hypertonus of his spinal and abdominal muscles, with slight opisthotonos, and hypertonus of the muscles of his right leg. He was given 240,000 units of antitetanic serum—200,000 units intravenously and the rest intramuscularly. On the day after admission the wound on his shin was excised.

For nine days from the time of admission the patient was kept more or less continuously under the influence of bromethol or paraldehyde. Bromethol per rectum was used for the first three days, an initial dose of 5.1 ml. of bromethol fluid being followed by a maintenance dose of between 2 and 3 ml. Following this, paraldehyde, in a 10% solution in saline, was given per rectum for six days in doses of 2 to 4 dr. (8–15 g.). The frequency of dosage with each drug (about every six hours) was governed by the patient's degree of somnolence. In all, 21.1 ml. of bromethol fluid and 57 dr. (200 g.) of paraldehyde were given.

From the start of treatment, in view of the anticipated prolonged sedation, 5% carbon dioxide inhalations for a few minutes, and coughing exercises, were given six-hourly.

During his first night in hospital, and again on the second day when his wound was being dealt with, the patient had a cramp-like exacerbation of his muscular spasm. By the third day his condition had deteriorated in spite of sedation. His body musculature was more rigid, and he was having a good deal of pain. He had a further exacerbation of spasm and was complaining of some difficulty in breathing.

It was then decided to try the effect of *d*-tubocurarine chloride. As we were uncertain of the degree of muscular paralysis which would be required to give relief, we brought to the ward a Drinker respirator and anaesthetic trolley with accessories. *d*-Tubocurarine chloride in solution was given slowly by the intravenous route, and after a dose of 8 mg. the patient's face relaxed, he remarked that his muscle pains were quite easier, there was some diminution in the spasm of his lumbar and abdominal muscles, and he was able to separate his incisor teeth 1 in. (2.5 cm.) compared with ⅓ in. (0.8 cm.) beforehand. Immediately afterwards a further 6 mg. of the drug was given by subcutaneous injection. After this we gave *d*-tubocurarine chloride in solution by intramuscular injection in doses ranging from 7.5 to 12.5 mg. every few hours, the frequency of administration being adjusted so as to control the pain and exacerbations of spasm. The patient received *d*-tubocurarine chloride for six and a half days at intervals of from two to six hours, the total amount given being 252 mg.

During this time he remained free from exacerbations of spasm and comparatively free from pain, except when the action of curare was wearing off. At these times severe interscapular, lumbar, and abdominal pain would recur, associated with increased hypertonus, cyanosis, and a rise in the pulse rate from about 80 to between 120 and 150 a minute.

By the ninth day in hospital the pain, spasm, and cramps were diminishing, and we stopped the administration of sedatives and curare. In the ensuing few days the residual stiffness wore off and he felt well and hungry. He lost 4 lb. (1.8 kg.) in weight during his illness.

On June 20 he wrote to us saying that he felt fit and was back at school.

We are reluctant to draw far-reaching conclusions from the treatment of one case, but we feel that *d*-tubocurarine chloride, when combined with other measures, may find a useful place in the treatment of tetanus.

We wish to thank Dr. H. Arwel Thomas, medical officer of health for Denbighshire, for permission to publish this case.

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Cardiac Arrest: Mod'fied Technique of Cardiac Massage

Cardiac massage has become standard treatment for heart failure during anaesthesia, and a number of lives have been saved thereby. On many occasions, however, the heart does not restart. The following case suggests that a modification of the technique advocated by Hamilton Bailey (1941, 1942, 1946) might be more successful.

CASE REPORT

A Bantu woman aged 19 was having a vaginal repair done for a vesico-vaginal fistula which she had had for 18 months following a difficult confinement in her village. She appeared to be in a satisfactory condition before the operation. Her heart seemed normal and she was not anaemic.

The operation was performed under gas, ether, and oxygen via an intratracheal tube. It had been in progress about half an hour, during which time there had been very little blood loss, when it was noticed that the oozing from the operation field was dark. This was reported to the specialist anaesthetist in charge, who at once increased the oxygen and stopped the ether and nitrous oxide, but without improvement in the patient's condition: the pulse and respiration were fading away. After a few minutes of artificial respiration the anaesthetist reported that the patient's heart had ceased beating, and that cardiac massage was indicated. Meanwhile artificial respiration by means of the anaesthetic bag was continued and an attempt was made to inject adrenaline into the heart. (After cardiac massage had been started it was considered that the needle could not have penetrated deep enough to reach the heart.)

A left subcostal incision was rapidly made and cardiac massage attempted without opening the diaphragm. After a fruitless minute an opening was made in the diaphragm and a thumb was passed through. Massage was then continued for a further eight minutes by rhythmically squeezing the ventricles. This procedure produced no results and the case was considered hopeless.

The hole in the diaphragm was then stretched somewhat and two fingers were passed through. By stretching the diaphragm upwards they could easily reach the upper parts of the heart. Then with some idea at the back of my mind of imitating the path of the normal impulses passing down the bundle of His, I stroked the heart firmly in a downward direction. It immediately responded with a weak beat, and after a few further strokings it was beating well. Natural respiration restarted shortly afterwards, and within five minutes the blood pressure was 120/85.

The patient, however, did not recover consciousness completely and showed evidence of cerebral damage. She became very spastic and made repeated infantile sucking movements. She would, however, open her eyes when called by name. Death occurred 30 hours after the heart had restarted beating.

It was felt that if this manœuvre had been tried earlier the outcome might have been more satisfactory. Perhaps it will prove useful to other surgeons placed in these unpleasant circumstances.

My thanks are due to Professor O. S. Heyns for his advice and help.

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Reviews

ASEPTIC TECHNIQUE

The Aseptic Treatment of Wounds. By Carl W. Walter, A.B., M.D. Illustrated by Mildred B. Codding, A.B., M.A. Macmillan Surgical Monographs. (Pp. 372. £2 5s.) New York and London: The Macmillan Company. 1948.

Asepsis is to-day so much the atmosphere in which the surgeon has his well-being that few of us spend many moments in thinking actively of its details. Our aseptic technique is so ingrained as to be a form of reflex behaviour rather than an intentional code of conduct. With the advent of chemotherapeusis, indeed, the miracle of asepsis is largely obscured by what is now the more dramatic miracle of the neo-antisepsis. It is a healthy, an instructive, and in some ways a humiliating experience for the surgeon to turn his attention to the full details of the aseptic methods as they are so admirably illustrated in this book, which covers in an almost encyclopaedic way the whole subject of asepsis. It would form an admirable textbook of asepsis for the medical student; it will serve the practising surgeon, however rigid and educated his technique, as a work of reference for numerous details of operating-room technique which are not available elsewhere.

The sterilization of the more modern materials, the packing of sponges and gowns for sterilization, the structure, management, and servicing of sterilizing apparatus, the management of the operating-room atmosphere, and the structure of hospital water supply are only a few subjects which are fully covered and delightfully illustrated by line drawings. The author discusses clearly the distillation and sterilization of water, the cleaning of glassware, and the preparation of fluid for parenteral administration and for blood transfusion, as well as the technique for achieving asepsis in the nursing of infectious fevers. He even considers operating-theatre technique to some extent, and describes the towelling of patients for various operative procedures, and methods of restraining them from breach of asepsis by their own movements. This is a most unusual volume, unique of its kind, and as a reference work must find a place in every hospital, however small, and in every medical library, however specialized.

IAN AIRD.

ENDOCRINOLOGY AND METABOLISM

The 1947 Year Book of Endocrinology, Metabolism and Nutrition. Endocrinology, edited by Willard O. Thompson, M.D. Metabolism and Nutrition, edited by Tom D. Spies, M.D. (Pp. 575; illustrated. $3.75 or 21s.) Chicago: Year Book Publishers, Inc. London: H. K. Lewis and Co. 1948.

This annual review is invaluable for those who have not the time to follow the original literature at first hand, and is particularly useful to the clinical endocrinologist, for the endocrine section is written by a clinician by no means lacking the scientific approach. In the section on the pituitary there is a review of the Boston School's demonstration of the *in vitro* inactivation of pituitary thyrotrophic hormone by iodine, due presumably to the formation of an iodo-complex of the hormone, which can be reversed by reducing agents, particularly goitrogenic ones; and an account of the work of Thorn and colleagues showing that adrenocorticotrophic hormone causes (particularly in hypopituitarism but also in normal man) an increase in the urinary excretion of 11-oxysteroids, 17-ketosteroids, uric acid, nitrogen, potassium, and phosphorus, with a decrease in sodium excretion.

A series of papers prove the usefulness of estimating protein-bound iodine in the serum as a reliable index of thyroid function, the low values seen in myxoedema and cretinism being more truly indicative even than the B.M.R. and serum cholesterol. A case of congestive heart failure due to myxoedema and responding to thyroid extract is described. Several papers on propyl thiouracil, which is the form used now in the U.S.A., in cases of thyrotoxicosis are informative. The interesting work of Rawson and McArthur is referred to—namely, on successive biopsies of the thyroid gland in thyrotoxicosis, showing that thiouracil increases slightly the height of the acinar cells, whereas if iodine is given with thiouracil the height is reduced to half its size. Radioactive iodine studies show that thiouracil prevents the thyroid gland from utilizing iodine when iodine

is also given. The authors believe that iodine can cause involution of the thyroid gland of the patient on thiouracil without iodination of the hormone precursor, and that the involuting action of iodine on the thyroid is independent of its iodinating action.

The section on the adrenal gland sets out the most interesting recent knowledge with skill and discrimination. In particular, the work of Venning and Browne at McGill University has turned our attention to the high excretion of glycogen corticoids (diabetogenic and anti-insulin) in Cushing's syndrome, and their tendency to disappear in Addison's and Simmonds's diseases. It is no longer sufficient to study only the 17-ketosteroids or androgens, and it is hoped that colorimetric methods of assay of glycogen steroids will be added to the assay by glycogen deposition in adrenalectomized rats and help to make the results of these studies more easily available to the scientific clinician. The account of hypertension in children due to phaeochromocytoma, their cure by its removal, and the diagnostic test of histamine injection will interest the paediatrician.

The work of an English paediatrician, Professor R. W. B. Ellis, on physiological standards of growth and puberty is rightly considered important to the endocrinologist in the section on the sex glands. Gynaecomastia associated with cirrhosis of the liver and due to inability of the liver to inactivate oestrogens is described. An account of twins with descent of one testis on opposite sides (mirror reflection type) reminds one of two eunuchoid brothers with similar unilateral descent shown by the writer at the Royal Society of Medicine (*Proc. R. Soc. Med.*, 1946, **39**, 511). The value of biopsy studies in male sterility is indicated. The importance of oestrogens and androgens in the osteoporosis of post-climacteric age and in the healing of fractures at this time should be better known to orthopaedic surgeons. Disorders of menstruation, synthetic oestrogens, and pregnancy tests are widely reviewed, as well as masculinizing ovarian tumours. The association of vascular damage, retinitis, and hypertension is discussed, as are the changes in mineral metabolism in diabetic coma; there is a wide range of clinical studies in therapy. A case of refractoriness in a young diabetic woman to 5,000 units of insulin in 24 hours is stated to be a record. An account of pancreatic islet-cell tumour hypoglycaemia and glycogen disease ends an excellent section on the pancreas. The second section of the book covers the alimentary tract, fat absorption in sprue, folic acid, the haemopoietic system, the cardiovascular system, the brain and nervous system, "agenized" flour, the genito-urinary system, and dermatology. The whole book is excellently set out and deserves high praise.

S. LEONARD SIMPSON.

DISORDERS OF SPEECH

L'Aphasie et la Désintégration Fonctionnelle du Langage. By Th. Alajouanine and P. Mozziconacci. (Pp. 156, illustrated. 450 francs.) Paris: L'Expansion Scientifique Française, 23 Rue du Cherche-Midi.

The literature on aphasia is outstanding by reason of the general high level of the contributions. Alajouanine and Mozziconacci's little work is a modest but distinguished newcomer. The authors follow the common practice of considering in some detail the history of the development of our knowledge of speech disorders—an approach which is of particular value in this subject. One or two features in the subsequent chapters will perhaps be unfamiliar to English students. They give due credit to Baillarger's teaching on the dissociation between voluntary and automatic (or spontaneous) utterances. There is a good account of the intellectual level of aphasics and the appropriate methods of investigation by means of non-language tests, and they consider artistic realization in aphasics in a brief but interesting manner. The authors relate aphasia to apraxia and the agnosias, the points of correspondence and of distinction being clearly discussed. One of the most important and at the same time original conceptions in the book is the study of aphasia from a philological viewpoint. Under the term "syndrome de désintégration phonétique" the authors discuss the elocutory disorders in aphasia, which they believe to have interesting analogies with the first usage of speech in the infant. Seven detailed illustrative case reports conclude this very successful monograph. From the point of view of the student and young neurologist there exists no better, clearer, or more up-to-date presentation of the subject.

MACDONALD CRITCHLEY.

BOOKS RECEIVED

[*Review is not precluded by notice here of books recently received*]

Liver Injury. Edited by F. W. Hoffbauer, M.D. (Pp. 95. $1.50.) New York: Josiah Macy. 1948.

Papers and discussion on such subjects as radioactive methionine, portal hypertension, the effect of plutonium on the liver, and serum lipids in liver disease.

Sterilisation und Sterile Aufbewahrung von Spritzen und Hohlnadeln. By E. Baumann. 2nd ed. (Pp. 120. 7.50 Swiss francs.) Basle: Benno Schwabe. 1948.

A monograph with references on maintaining sterility of syringes and hypodermic needles.

Income Tax Simplified. By A. and E. E. Fieldhouse. 19th ed. (Pp. 98. 2s. 6d.) London: Simpkin Marshall. 1948.

A short exposition specially for the business man and student of accountancy.

The Medical Annual 1948. Edited by Sir H. Tidy, M.A., M.D., F.R.C.P., and A. Rendle Short, M.D., B.S., B.Sc., F.R.C.S. (Pp. 414. 25s.) Bristol: John Wright. 1948.

Articles by various authorities on modern treatment in medicine and surgery, with references to the literature.

Aetiological Principle of Pyaemia in Ancient Egyptian Medicine. By R. O. Steuer. (Pp. 36. $1.50.) Baltimore: Johns Hopkins Press. 1948.

A short study issued as a supplement to the *Bulletin of the History of Medicine.*

Annual Review of Biochemistry. Edited by J. Murray Luck. Vol. 17. (Pp. 801. 36s.) London: H. K. Lewis. 1948.

Includes papers on the chemistry of penicillin, lipid metabolism, clinical application of biochemistry, and the biochemistry of carcinogenesis.

Nouveaux Traitements de L'Insuffisance Hépatique. By J. Cottet and N. Dobo. (Pp. 210. No price.) Paris: Flammarion. 1948.

A discussion of the diet and its constituents required for treating hepatic disorders.

Der Ausdruck von Stimme und Sprache. By F. Trojan. Vol. 1. (Pp. 219. Sch. 25.) Vienna: Wilhelm Maudrich. 1948.

An analysis of speech for phoneticists and speech therapists.

La Spasmophilie de L'Adulte. By H. P. Klotz. (Pp. 157. No price.) Paris: Flammarion. 1948.

The author describes a syndrome of neuromuscular and mental hyperexcitability with hypocalcaemia.

Corazon Pulmonar. By J. Govea. (Pp. 178. $4.00.) Havana: M. V. Fresneda. 1948.

A monograph on pulmonary heart disease.

Lehrbuch der inneren Medizin. By T. Brugsch. Vol. 1. (Pp. 764. M. 40.) Berlin: Urban and Schwarzenberg. 1947.

This volume includes sections on infectious diseases, physiotherapy, disorders of metabolism, and the cardiovascular system.

The Queen Charlotte's Textbook of Obstetrics. By Members of the Clinical Staff of the Hospital. 7th ed. (Pp. 572. 28s.) London: J. and A. Churchill. 1948.

This edition includes new chapters on foetal physiology and the rhesus factor.

Les Varices et leurs Associations Pathologiques. By L. Gerson. 2nd ed. (Pp. 259. 850 francs.) Paris: G. Doin. 1948.

A clinical account of the treatment of varicose veins and ulcers.

Critical Studies in Neurology. By F. M. R. Walshe, M.D., F.R.S. (Pp. 256. 15s.) Edinburgh: E. and S. Livingstone. 1948.

Includes papers on the anatomy and physiology of cutaneous sensibility, the motor cortex and pyramidal tract, and the notion of the "discreet movement" in willed motion. Reprinted from *Brain*, with a lecture on the integration of medicine reprinted from this *Journal.*

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STREPTOMYCIN RESISTANCE IN TUBERCULOSIS

The Achilles heel of streptomycin is acquired bacterial resistance. All species are liable to develop this to a degree which renders further treatment quite fruitless, and the rapidity with which it occurs varies with their rate of growth. Resistance has been observed only one day after the start of treatment, and it is quite common among most bacteria within two or three days. The slowly growing tubercle bacillus, on the other hand, has not usually been found to react in this way in less than one month. The frequency, extent, and rate of this change are of vital importance in deciding how to treat tuberculosis with streptomycin, particularly in connexion with the length of the course. In cases of pulmonary tuberculosis the sputum often continues to provide experimental material, and several studies of resistance have been made. Sadusk and Swift[1] found that out of 16 cases, 14, 11, 7, and 6 respectively still had bacilli after one, two, three, and four months of treatment. Only 2 strains had begun to be resistant after one month; after two months, 7 out of 11 were resistant; after three, 6 out of 7; and after four, all 6. The degrees of increase in resistance varied from 5- to over 1,000-fold. These authors were not able to correlate the behaviour of the bacilli with the response to treatment. On p. 1009 of this issue Drs. J. Crofton and D. A. Mitchison describe a similar study in 13 patients at the Brompton Hospital, the results of which are carefully analysed in an attempt to arrive at such a correlation. In 12 out of 13 patients the bacilli were shown to have increased in resistance, and in two-thirds of them this change occurred within 48 days. With one exception the change was of such a degree that the concentration of the drug attained in the tissues can no longer have been capable of preventing the growth of such bacilli.

Several conclusions can be drawn from the details of these findings. The sooner resistance develops, the greater is its ultimate degree. The amount of clinical improvement during the early stages of treatment is also related to this factor, patients in whom resistance develops late and to a limited extent making better progress. It also appears that the development of resistance is apt to be followed by an increase in the numbers of bacilli in the sputum. On the other hand, the development of resistance is by no means invariably followed by clinical deterioration: 8 patients continued to improve after the change had occurred, 2 continued to deteriorate having been on this road before, and in only 3 was progress arrested or reversed. The authors' discussion of the significance of these facts and of the further questions which arise will be read with interest. As the facts stand they are by no means unaccountable. There is much to be said for the view that all the good that streptomycin can do is going to be done in six or eight weeks. If at the end of that time the destruction of the bacilli and the resolution of lesions have reached a certain stage improvement may well continue even though continued administration of the drug is having no effect whatever on the surviving bacilli.

It would be useful if further studies of this kind could be pursued on a larger scale, but anyone undertaking them has to face a formidable task. Apart from the ordinary difficulties in working with a fastidious and slow-growing organism a special difficulty in this connexion is the heterogeneity of the bacterial population. There appears to be no doubt that resistant organisms are derived from mutants originally possessing some degree of abnormal resistance, and there may well be small numbers of these in any population. This has been clearly shown by Alexander and Leidy[2] for *H. influenzae* and by Klein and Kimmelman[3] for dysentery bacilli. Vennesland and his colleagues[4] have even shown that the classical strain of *Myco. tuberculosis*, H37Rv, commonly used as a control in tests of streptomycin resistance, includes a minute proportion of cells capable of growth in 100 times the normal inhibitory concentration. Under the influence of streptomycin it seems that individual cells acquire resistance at different rates, and a population develops which includes elements possessing widely different degrees of resistance. Crofton and Mitchison demonstrated this in two of their cases, and it is abundantly evident from the elaborate study made by Marjorie Pyle,[5] who repeatedly cultivated the organism obtained from the sputum of patients under treatment on plates of a medium containing seven different concentrations of streptomycin, often obtaining a diminishing number of colonies over a considerable range of concentrations. If such a procedure as this is not adopted it must always be uncertain how far a result reflects the properties of the majority of bacilli in the specimen. Finally, there is some uncertainty about the significance of results obtained with the Davies-Dubos medium. This is delightfully convenient to work with, but according to Fisher[6] one of its constituents, Tween 80, greatly exaggerates the bacteriostatic action of streptomycin on some strains, making them appear sensitive when in fact they are highly resistant as judged by tests in other media. This of course does not detract from the significance of results in which a high degree of resistance has been demonstrated.

It is clear from Crofton and Mitchison's findings that the development of streptomycin resistance is not incompatible with recovery: three out of their cases with resistant bacilli became sputum-negative. On the other hand, it is equally certain, though so far as we know not yet actually proved, that such bacilli if transmitted to another individual would produce disease resistant to streptomycin treatment from the start: there would be none of the benefit obtained in the first patient before resistance had been acquired. This is a very grave danger for the future,

1 *J. clin. Invest*, 1948, **27**, 278.
2 *J. exp. Med.*, 1947, **85**, 329, 607.
3 *J. Bact.*, 1946, **52**, 471.
4 *Science*, 1947, **106**, 476.
5 *Proc. Mayo Clin.*, 1947, **22**, 465.
6 *Amer. Rev. Tuberc.*, 1948, **57**, 58.

and the strongest of several reasons for restricting the use of streptomycin to those types of case most likely to benefit from it. The result of making the drug more widely available will be an insistent demand for it from many patients in whom its use is unlikely to have any but a transient effect, and it will be the duty of the profession to resist such demands firmly. To treat a chronic advanced case with cavitation can have little effect but to convert the patient into a much more dangerous source of infection for other people. There is no evidence whatever that a tubercle bacillus—or indeed any other organism—which has acquired streptomycin resistance can lose it again. So far as is known the change is permanent.

EARLY RISING AFTER OPERATION

To make patients get out of bed a day or two after operation is not a new idea, and though this practice is rapidly becoming more popular there is still considerable opposition to it in many parts of Britain. Emil Ries[1] is reputed to have been the first advocate of early post-operative ambulation in America. His paper was presented at a meeting of the American Medical Association in 1899 and was given a most favourable reception by all the succeeding speakers except one. It is, therefore, rather surprising that Ries's advice was not widely accepted. Perhaps it was because tradition and habit die hard in medicine, and this is especially true of methods sanctioned and advocated by great authorities. In this country we have not lacked distinguished supporters for the therapeutic importance of rest: John Hunter described it as the most powerful aid which the surgeon could bring to disordered tissue; Hugh Owen Thomas stated that "rest must be enforced, uninterrupted, and prolonged"; and there are few of us who were not advised as students to read the classical essays of Hilton.[2]

Up to 1939 confinement to bed for ten to fourteen days after a major operation was the usual custom in this country and the United States. Continental practice was more adventurous, and early rising was occasionally advocated in Russia and Germany in a manner which many considered almost barbaric. But shortage of hospital beds during the war and the pressing demands on manpower encouraged a change of view, and there is now a growing and enthusiastic body of supporters of early post-operative ambulation. The majority of patients can readily get out of bed by the third or fourth day after operation, and many of them might with advantage get up even earlier. There is more than historical interest in the fact that Dr. Ephraim McDowell, who did the first successful ovariotomy in 1809, found his patient up making her bed on the fifth day after operation.[3]

What are the benefits of early ambulation? First, morale is greatly improved by early rising, and most patients, having overcome their natural apprehension, are gratified to find how comfortable and fit they are. General health and strength are better maintained, and convalescence is more rapid. Secondly, retention of urine, together with those difficulties associated with the use of the bed-pan, is almost entirely obviated, and the work of the nurses is made easier. For patients who are not fit enough to walk to the lavatory the wheeled chair described by Bohmansson and Malmros,[4] which can be pushed over a w.c., is of considerable value. The patient is thereby spared embarrassment and discomfort, while his neighbours avoid those unpleasant odours which are commonplace in hospital wards. Thirdly, as many authors have reported,[5-10] early ambulation diminishes the incidence of post-operative pulmonary collapse, and if collapse does occur it generally resolves more rapidly. Churchill[11] demonstrated an appreciable reduction in the vital capacity after abdominal and hernia operations, while Cutler[12] has shown that the vital capacity returns to normal in half the time if the patient is up and active. As a result of studying the diaphragmatic movements after operation Howkins[13] concluded that so long as the patient had to remain in bed he should be in a comfortable recumbent position with free and frequent movement. Like Spalding,[14] he condemns the Fowler position and advocates early ambulation wherever this is possible. Finally, most workers believe that venous thrombosis and its sequelae are not so likely to occur if early rising is practised.[15-17] According to some reports these complications are lessened tenfold, but most authorities find that the incidence is not reduced by much more than half.[18] It is suggested by others that rising on or after the fourth post-operative day produces little or no diminution in thrombosis and embolism; the greatest reduction in these complications appears to occur when patients get up on the first or second day after operation.

The abdominal surgeon's chief anxiety about early rising has been the integrity of his suture line, and wound disruption and post-operative herniation were much feared. For these reasons metallic sutures, and especially stainless steel wire, have been advocated,[5 19] but operation wounds will heal rapidly and securely even without such desirable aids as non-absorbable sutures. Royster and his co-workers[20] showed that wound healing was as sound in ambulant dogs as in those which had been kept inactive, and Newburger[21] found that wounds healed more rapidly in ambulant rats, thus confirming the earlier work of Kimbarovsky.[22] Experience with human patients supports these findings. There is no published evidence that early rising increases the recurrence rate of inguinal hernia.[23 24]

Contraindications to early ambulation after operation are peritonitis, severe ileus, shock and haemorrhage, cardiac failure, and infective conditions of the legs which preclude

1 *J. Amer. med. Ass.*, 1899, **33**, 454.
2 *Rest and Pain*, 1892, George Bell and Sons, London.
3 Haggard, W. D., *Surg. Gynec. Obstet.*, 1934, **58**, 415.
4 *Lancet*, 1947, **2**, 509.
5 Booth, J. D., *Conn. med. J.*, 1947, **11**, 609.
6 Deming, C. D., ibid., 1947, **11**, 611.
7 Cornell, N. W., and Lin, D. T. W., *Surg. Gynec. Obstet.*, 1947, **85**, 294.
8 Davison, T. C., *et al.*, *J. med. Ass. Ga.*, 1947, **36**, 299.
9 Leithauser, D. J., *Arch. Surg.*, 1943, **47**, 203.
10 Leithauser, D. J., *et al.*, ibid., 1941, **42**, 1086.
11 *Surg. Gynec. Obstet.*, 1927, **44**, 483.
12 *Proceedings of the International Assembly of the Inter-State Postgraduate Medica Association of North America*, 1941, p. 232.
13 *Lancet*, 1948, **2**, 85.
14 Ibid., 1946, **1**, 643.
15 Iorpes, E., *Heparin in the Treatment of Thrombosis*, 1946, Oxford University Press, London.
16 Crafoord, C., Personal communication, 1947.
17 Ochsner, A., *J. Amer. med. Ass.*, 1946, **132**, 827.
18 Allen, A. W., *et al.*, ibid., 1945, **128**, 397.
19 Abel, A. L., and Hunt, A. H., *British Medical Journal*, 1948, **2**, 379.
20 *Surg. Gynec. Obstet.*, 1948, **86**, 565.
21 *Surgery*, 1943, **13**, 692.
22 *Nov. khir. Arkh.*, 1935, **35**, 57.
23 Blodgett, J. B., and Beattie, E. J., *Surg. Gynec. Obstet.*, 1947, **84**, 716.
24 Pratt, G. H., ibid., 1948, **86**, 530.
25 *British Medical Journal*, 1947, **2**, 967.

such activity. It is sometimes argued that early rising is undesirable for the tired housewife who needs nothing so much as a good rest in bed. The reply to this is that the housewife need not be strictly confined to bed in order to enjoy a well-earned rest. A very real danger associated with the practice of early rising is the too early discharge of the patient from hospital; this must be strongly resisted. On a number of occasions early discharge from surgical care has been followed by fatal embolism or the development of a "white leg" when the patient was back at home. Some of the undoubted benefits of early ambulation will be lost and the practice brought into disrepute if it leads to neglect of the need for a period of close and careful post-operative supervision. A surgeon would be in a difficult position if he allowed a patient to be discharged on the fourth day after appendicectomy or the seventh day after cholecystectomy (as reported in some American journals) and that patient subsequently developed a fatal embolus in the second week. Although no definite time limit can be set for the development of serious thrombotic complications, it would be wise to keep the patient in hospital for fourteen days after any major operation.

Early ambulation should not be regarded as a procedure to be practised only by surgeons. Patients transferred from a medical to a surgical ward are sometimes found to be suffering from the effects of prolonged bed rest, and it may well be prudent for the surgeon to get such patients up and about for a few days before operation. The dangers of going to bed were described in this *Journal* about a year ago by Asher,[25] who drew attention to the need for changes in wards. Those who recommend early rising after operations will realize the defects of even the most modern hospitals in this respect. There is a serious shortage of comfortable chairs, and most patients would appreciate an adjacent sitting-room or recreation room. Washing and bathing facilities for up-patients are usually inadequate and there is a shortage of lavatories. Those responsible for hospital planning should bear these points in mind when new hospitals are built and existing institutions improved.

DIET AND THE PRODUCTION OF INSULIN

There have been suggestions that diabetes mellitus is particularly prevalent among those who are accustomed to an unduly generous diet or to consuming large amounts of sugar or fat. While statistics indicate that diabetes is commonly associated with obesity, the evidence connecting its development with excess of a particular food component is less convincing. Thus, while it has been claimed that heavy fat-eaters are frequently affected,[1] it is questionable whether the appetite for fat is developed before or after the pathological changes have begun. Tejning[2] has recently carried out a series of experiments with the object of throwing some light on this important question. He kept groups of rats for about nine months either on a stock diet of rye, meat, milk, and carrots or upon experimental diets rich in carbohydrate, protein, or fat, respectively. The animals were then killed and their pancreases were carefully fixed and freed from adipose tissue. By examining sections cut under carefully controlled conditions and by the application of complicated and laborious mathematical methods estimates were made of the number, size, and total volume of the islets of Langerhans in the animals of the various groups. Although the insulin contents of the islets were not examined it was assumed, since no pathological changes were found, that the total volume of the islets would give a true indication of the demand made by the diet on the production of insulin.

When the total volumes of the islets were calculated per 100 g. of body weight the values for males and females in the group given the natural diet were 0.67 and 0.74 c.mm. respectively. With the high carbohydrate diet the corresponding values were 0.71–0.89, with high protein 0.59–0.68, and with high fat 0.47–0.50 c.mm. If the volume calculated in the group of rats on the natural diet is accepted as normal the diet rich in carbohydrate had little apparent effect on the islets. Their volume, however, was lowered by the diet rich in protein, while the diet rich in fat produced an even greater decrease. Some caution seems necessary in the interpretation of these findings. It is surprising that while the average body weights of male and female rats fed on a diet rich in carbohydrate were 306 and 194 g. respectively, weights of only 224 and 168 g. were reached with a natural diet. Most workers have found that even when all known vitamins and other nutrients are supplied rats usually grow less rapidly upon artificial than upon natural diets. Further, while the diet high in carbohydrate contained an adequate amount of protein for maximum growth and was well balanced between these types of foodstuff, the diet rich in protein was a "freak" diet containing about 90% of casein. There is some evidence that such a high intake of protein is injurious, and the ability of the rats to grow to 227 and 169 g. and so equal the performance of the rats upon the natural diet is again hardly what might have been expected. The growth of the rats receiving 76% of their calories as fat to weights of 265 and 194 g. calls for the same comment.

It is probably reasonable to accept the hypothesis that the islet tissues respond to dietary changes. It is more doubtful, however, whether the effects of the diets used should be ascribed directly to their richness in carbohydrates, protein, or fats and not to secondary effects on the food consumption and on the general health of the animals. Experiments in which body weights of the rats given the diets rich in carbohydrates and fats could be kept down by restriction of the intake of food to the levels found in the other groups might give useful information on this point.

[1] Himsworth, H. P., and Marshall, E. M., *Clin. Sci.*, 1938, **2**, 103.
[2] *Acta med. scand., Suppl.* 198, 1947, **128**.

ACUTE CORONARY INSUFFICIENCY

Angina pectoris has come to mean an attack of pain in the chest which has a particular quality, site, radiation, duration, and relation to effort, and which is caused by or is closely connected with transient ischaemia of the heart muscle. Cardiac infarction or myocardial infarction signifies necrosis of a substantial segment of heart muscle and is associated with equally well-known clinical features. It is usually but not invariably due to coronary thrombosis. Coronary occlusion, thrombotic or otherwise, means no more than its literal sense implies: it may or may not cause cardiac infarction. So much is clear. What is not so clear is the classification and underlying pathology of those conditions which are neither angina pectoris (as defined above) nor cardiac infarction, but something between the two. Master and his colleagues[1] have proposed the term "acute coronary insufficiency" to describe such cases. The physiological basis for the condition is similar to that

[1] *J. Mt Sinai Hosp.*, 1947, **14**, 8.
[2] Wiggers, C. J., *Amer. Heart J.*, 1947, **33**, 633.
[3] Sharpey-Schafer, E. P., *Brit. med. Bull.*, 1944, **2**, 171.

for angina pectoris, but the contributing factors may have been present for a relatively long time. For instance, prolonged increase of cardiac work may be due to paroxysmal tachycardia, auricular flutter, hypertensive crises, thyrotoxic crises, and certain drugs, such as an overdose of adrenaline. Prolonged diminution of the coronary blood flow may be due to conditions which seriously lower the cardiac output and blood pressure, such as haemorrhage, shock, massive pulmonary embolism, and vasovagal syncope. Prolonged and relatively sudden interference with the oxygen content of the blood occurs in asphyxia, carbon monoxide poisoning, and acute anaemia. In all these conditions the nutritional demands of the heart may not be adequately met, and subendocardial necrosis in any part of the left ventricle may result. It is believed that the necrosis occurs at this site because of the intramyocardial pressure gradient during systole.

The signs and symptoms may resemble those of cardiac infarction or angina pectoris, but more often they are not quite like either, being too prolonged for ordinary angina, yet without many of the features of infarction. Sometimes acute coronary insufficiency is clinically silent. The electrocardiogram shows depression of the RS–T segment in all left ventricular surface leads and therefore usually in all standard leads. The same pattern is common during an attack of classical angina pectoris and may be found in normal individuals when breathing 10% oxygen. Although this conception of Master's has been recognized in some quarters for a long time it is not widely known or accepted, yet there is much to recommend it. Acute coronary insufficiency is believed to be responsible for the occurrence of true heart failure in the later stages of shock[2] and may explain the readiness with which heart failure develops during transfusions in the hyperkinetic stage of severe haemorrhage or anaemia.[3]

ANTIHISTAMINE DRUGS AND GASTRIC SECRETION

When antihistamine compounds were introduced and found to relieve hay-fever and urticaria, the hope arose that they might be of use in treating hyperchlorhydria, particularly in patients suffering from gastric ulcer, whose gastric juice often resembles the secretion produced by the injection of histamine. This hope has been disappointed, and indeed evidence is accumulating that some of the antihistamine compounds increase the secretion produced by histamine. Emmelin and Frost[1] found that in cats "benadryl" increased the secretion of gastric juice in response to histamine and that in three cats out of four the administration of benadryl alone, without histamine, had a stimulating effect on secretion. Doran[2] observed a large increase in the secretion of free acid in patients given benadryl as compared with the amount secreted without the drug. Benadryl is not a highly specific antagonist of histamine, since it antagonizes acetylcholine as well; this explains the occasional dryness of mouth which it causes. "Neoantergan" (or "anthisan") has a more specific and stronger action against histamine, and it might have been reasonable to suppose that its effect would differ from that of benadryl. But Howat and Schofield[3] have found that it too acts like benadryl and increases the secretion produced by histamine. Wood[4] has also examined its action in cats and has confirmed Howat and Schofield's findings. The slow intravenous infusion of a mixture of 15 μg. anthisan and 5 μg. histamine per minute for a period of five hours doubled the volume of juice and rather more than doubled the amount of free HCl secreted in each 30-minute period. Only when the anthisan was reduced to one-third and the histamine increased four times was there any indication that the secretion of acid was less than with the same amount of histamine alone. It seems that further observations should be made to see whether smaller doses of these antihistamine substances may have the opposite effect to that which has been recorded by all observers hitherto, who, it should be noted, have all used high doses. It is strange that on gastric secretion alone there has till now been no suggestion of antagonism between substances which are antagonists everywhere else. It is likely that there is some simple explanation of this anomaly, which should well repay exploration.

1 *Acta physio. scand.*, 1947, **13**, 75.
2 *Lancet*, 1947, **2**, 490.
3 *J. Physiol.*, 1948, **107**, 30P.
4 *Brit. J. Pharmacol.*, 1948, **3**, 231.

OVERCROWDING IN MENTAL HOSPITALS

While there has been some recovery from abnormal conditions due to the war, there is still a great deal of overcrowding in public mental hospitals. The report of the Board of Control[1] for 1947 shows that with 128,517 patients in such hospitals there was overcrowding, on the basis of recognized standards, to the number of 14,668. The shortage of accommodation is due to the fact that there has been virtually no building since 1939, to the continuing diversion of some thousands of mental hospital beds to wartime purposes, and to the shortage of nursing staff. The number of beds not in use owing to staff shortage is close upon 2,000, but the shortages are highly localized, and in some parts of the country hospital staffs are nearly at full strength.

The inadequacy of accommodation is more serious than the mere figures suggest, because many mental hospitals have limited admissions to certified cases and have declined to receive voluntary patients—a policy which is clearly detrimental to the whole system of voluntary treatment and causes hardship to persons who voluntarily seek treatment, often in the early stages of their illness, when there is the best prospect of recovery. Nevertheless, voluntary admissions continue to show progress in relation to certified admissions, and last year represented 54.5% of the total. The report states that the health of the patients has been generally good, though there has been a slight increase in tuberculosis (8.8 per thousand, as against 6.5 the previous year and 8.1 as the ten-year average). Among methods of treatment special reference is made in the report to occupational therapy, which has gained wide acceptance in every kind of hospital and is a firmly established form of treatment in mental deficiency institutions for patients of all grades. The report adds, however, that "there are still few hospitals where it can be said that full opportunities are offered to patients as individuals or as members of groups for indoor or outdoor activities which may alleviate illness and point the way to health."

The number of admissions to mental hospitals in 1947 was 46,471. Those discharged recovered or relieved numbered respectively 15,243 and 14,491; 4,002 were discharged not improved and 10,595 patients died. These numbers do not include persons suffering from mental disorder in public assistance institutions and public health general hospitals, or those in receipt of outdoor relief, on whose movements there is no detailed information. Tables are appended to the report with the patients arranged according to class, as private, rate-aided, or criminal, and according to status, whether voluntary, temporary, or certified. The "temporary" patients are very few, only 110 males and 436 females. Rate-aided patients are ten times as numerous as private patients.

1 *Annual Report of the Board of Control to the Lord Chancellor for the Year 1947.* London: H.M.S.O. 2d. net.

TREATMENT OF ADVANCED RHEUMATOID ARTHRITIS

A FEW PRACTICAL POINTS

BY

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The prognosis of advanced rheumatoid arthritis is nearly always described as being bad. The later stages of the disease are often considered as untreatable. In a recent meeting of the Section of Physical Medicine at the Royal Society of Medicine which was devoted to the treatment of this disorder none of the speakers referred to the advanced stages of the disease. Poynton (1931) has said, "When the atrophic shrivelling of the tissues supervenes, we realize that recovery of the affected parts is not possible." In fact, most writers use words reminiscent of Dryden:

> For all the happiness mankind can gain
> Is not in pleasure, but in rest from pain.

In the geriatric unit at St. John's Hospital, Battersea, a series of patients of this type have been treated during the past year. By means of a combined assault on the disease the team of nurses, physiotherapists, physician, orthopaedic surgeon, and occupational therapist have been able to make some progress in the majority of cases. Several lessons have been learnt; these are put on record here in the hope that they will benefit others.

Preliminary Assessment

This is a very important part of the procedure. After a general physical examination a structural and functional survey of the locomotor system is carried out. It has been realized that a deformed joint can be useful and that a few degrees of movement may form a basis for therapeutic exploitation. *X*-ray reports on the state of the joints are not given great prognostic weight, for many cases with alarming skiagrams have been capable of clinical improvement. All the patients in the unit have several joints affected, so that the question of priority in treatment is an important one. As a general rule it has been the practice to start with the worst non-ankylosed joint. When both arms and legs are involved walking is considered more vital than manual efficiency; but this is not an invariable decision. Where the arthritis is complicated by another disease this should be dealt with first or therapy will be ineffective. Such conditions as renal calculi, gastric ulcers, fibrositis, and various psychological disorders have all caused either temporary or permanent lack of response to anti-arthritic treatment. It is essential to get a good social history, for there are some patients who, on account of domestic trouble or lack of a home, do not want to leave the shelter of hospital. Such patients need help from the almoner, social welfare workers, and others before any great advance can be made. They use arthritis as a shield against responsibility.

Procaine Lactic Acid

The injection of procaine lactic acid (P.L.A.) into and around affected joints has been the first line of attack in all the cases treated. The technique has been described elsewhere. A few minutes after injection the joints are manipulated. Some cases benefit most by a sudden jerk, others do better with steadily increasing pressure. There is probably a maximum to the number of joints which can be manipulated at one time. So far I have never done more than seven, but some patients feel faint if more than three are stretched. A great deal depends on the number of adhesions and the state of the joint capsule. Crepitus alone is not an indication that pain is liable to follow. A rubbing or dry grating like that of leather on a glass surface is a warning of pain to come if too much pressure is exerted. Sometimes the sensation experienced as the needle goes into the joint may be a guide. A feeling as of hard nougat is often associated with much pain during the injection, so that the patient finds it hard to relax afterwards. It is thought that this sensation means the puncture of cartilage. Fibrous tissue grips the needle, is painful on injection, and may hold the point when the syringe is withdrawn. This often detaches needle from barrel and causes patient and onlookers to get a shower-bath. Unless this hard fibrous tissue is properly penetrated the fluid stretches it painfully, so that the patient does not relax fully when manipulated. On the other hand, if the joint cavity has been properly injected subsequent movement is not difficult. Extreme distension of the joint cavity is painful, but is often followed by clinical improvement. Snapping or cracking sounds in a joint which is being manipulated are not always indications of mobility, although they impress the patient. Rupture of an adhesion seems to cause a single noise followed by increased movement. When bleeding has followed injection, post-manipulation pain often lasts longer than normal. Yet this haemorrhage is usually found in joints which are improving, so should not be regarded too seriously.

In two cases procaine has been used in place of P.L.A. Diminution of pain, increase of mobility, and decrease of crepitus are less marked in these patients than in those who have the acid injections. Procaine is most useful where dislocation or subluxation of a joint has occurred and where local muscular tender spots are found. In these two instances it seems preferable to P.L.A. A few patients are found who dread the needle-prick and who cry or moan when injected. When this miserable state is pronounced the administration of "allonal" tablets (Roche), "somnaseds" (Duncan Flockhart), or bromide half an hour before the treatment is a useful measure. It is important to have a relaxed and, if possible, co-operative patient to obtain the best results.

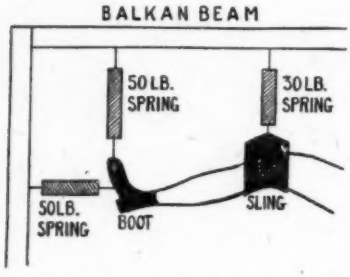
Treatment

Physiotherapy.—In conjunction with the injection therapy physical methods of treatment are also used. Owing to lack of staff and equipment in the chronic hospital which houses the unit, heat was perforce administered only in the form of infra-red rays and of paraffin wax. This was carried out twice a week as a routine, but some patients occasionally had periods of intensive treatment daily for a week or ten days. A few cases had ultra-violet light. Increase of mobility was the patients' primary need, and this was promoted by class-work in remedial exercises. The spirit of competition which this engendered had an excellent effect on the morale of the patients as well as their mobility. The ward sisters visited the classes from time to time. They observed that almost every patient was capable of much more exertion than expected from their usual behaviour. This resulted in making these cases less dependent on help from the nursing staff than previously. I also learnt a great deal from watching my patients doing their exercises. As a guide to the joint most urgently needing treatment this procedure could hardly be excelled; as a measure of the response to therapy it was admirable.

Occupational Therapy.—It was realized that manipulation once a week and exercises twice or three times a week would not be enough to maintain any increased mobility in stiff joints. The use of faradism had definite limits in such cases as these, so occupational therapy was encouraged and developed. First of all, knitting was prohibited; for many an arthritic had knitted day in and day out for many years, steadily getting stiffer all the while. Secondly, all forms of occupation were allocated on prescription only. Knotting and basket work for fingers, heavy looms for elbows and shoulders, table looms or leather work for wrists, were tried as a start. Rug-making and toy-making have been added, while patients are encouraged to do some of their work in the wards as well as attending the department twice weekly. There is nothing novel in all this, but the results were better than expected in the chronic arthritics who had never done this type of work before and who were depressed from sitting all day in the same ward week after week.

Orthopaedics.—The work of the orthopaedic surgeon is a necessary adjunct to the work on chronic arthritic patients: so many of the cases have multiple deformities through lack of adequate treatment in the past. Manipulation, together with serial plasters and other splintage, has done much to remedy the "hopeless" position of so many limbs. When contracted knees have been straightened, walking exercises in a machine

or at the foot of the bed can begin. The outlook of the patient is radically altered by such procedures. One danger must be mentioned, however. The bones of most arthritic patients are decalcified and fragile. It is easy to cause a fracture by over-enthusiastic manipulation, especially under a general anaesthetic. One problem which has not been solved is that of



deformed fingers with ulnar deviation and some subluxation. The use of paraffin wax followed by faradic stimulation gives some increased mobility, but not very great improvement. A recent development has been the use of springs with Guthrie-Smith slings and a special shoe to allow traction of contracted legs (see diagram). This is giving promising results, but is probably capable of further modification and improvement.

Results

Let us first take the three failures. One patient refused to have injections after a month's experience. Another was improved to the stage of starting to walk after being in bed for two years. Her arthritis was not severe in degree, but she used it as a means of escape from the difficulties of life outside hospital and did not wish to be cured. The third patient was suffering from a psychosis, which became worse during treatment.

As a contrast three patients who were bedridden a year ago are now able to walk and to dress themselves. One, a man aged 70, needed three nurses to carry him to the bath. He had severe arthritis of both shoulders, both elbows, both wrists and hands; the knees were also involved to a less extent. He can now walk, although his knees are still slightly bent. Both shoulders move freely and the elbows have increased flexion. The left wrist has become mobile instead of being fixed in a flexion deformity. The *x*-ray film shows little change, but the functional alteration is immense, for the patient can now go to stay with his daughter for a week-end, needing little help to live a normal life.

The man in the next bed had both shoulders, knees, hips, and elbows involved. He had been bedridden for two years before treatment and was also blind. For six months he gave no response to weekly treatment. Then quite suddenly he began to improve. He can now walk a little, dress himself, raise both arms above his head, and extend the left elbow better than before. He has learnt to take himself to the lavatory, and consequently needs little nursing attention. The left hip still shows limitation of movement, but this joint has had only a month's treatment so far.

The third patient, a woman, had also been bedridden for two years. She had both shoulders, elbows, fingers, and knees affected, with considerable limitation of movement. She can now walk and raise both arms level with her shoulders. The elbows retain a slightly flexed position. The left one was manipulated to increase extension, but this procedure resulted in no increase of movement. The arc through which the joint moved was merely transferred nearer extension, while a portion of the previous ability to flex was lost. Consequently the patient can no longer do her own hair.

Seventeen other cases have been treated for periods varying from one month to a year. All show some increase of joint movement. One patient whose hands and wrists were involved has been discharged to her home and can do her own housework. Two remain bedridden still, but one of these had twenty-six years without treatment before coming to our notice. Both her arms have been mobilized successfully, but the legs show great deformity. As she is a frail old woman of 74, the orthopaedic surgeon feels unable to undertake extensive operative treatment. Her neighbour of 60, who was without treatment in bed for twelve years, is improving steadily. Although both shoulders, hands, and knees are seriously affected she has recently become able to feed herself after five years, and the knees have now started to flex again. Another woman, whose knees appeared to be ankylosed, has just begun to get flexion in them after eleven months of regular weekly injections with P.L.A. It is surprising how often weeks of apparently fruitless effort will suddenly and unexpectedly produce results. At the moment it appears to me that few cases of rheumatoid arthritis are too advanced to benefit from treatment.

Summary

An account is given of the methods of treatment used for advanced rheumatoid arthritis at St. John's Hospital, Battersea.

The results of a year's use of procaine lactic acid are described.

Apart from three patients with abnormal psychology, all those treated in this way have shown some degree of improvement. Several patients who were previously bedridden are now ambulant.

It is sometimes necessary to wait several months before a patient will show response to the treatment.

It is suggested that this therapeutic procedure has improved the prognosis of advanced rheumatoid arthritis.

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OPHTHALMIC SURGERY ABROAD

FACULTY OF OPHTHALMOLOGISTS

Between the two world wars several visits by groups of ophthalmic surgeons to European and American clinics were organized by the late Percival Hay, of Sheffield, on behalf of the North of England Ophthalmological Society. The idea has been taken up afresh by the Faculty of Ophthalmologists, and in the spring of 1948 three parties of twenty surgeons visited Holland, Switzerland, and Paris. The travellers are unanimous in their praise of the courtesy they received at all the centres visited. Instruction and information on special techniques and research were freely given, evidently after careful preparation, and the social side was well catered for.

The party to Holland was organized and led by Mr. John Foster, of Leeds. Visits were made to The Hague (Dr. Vos), Scheveningen, and the old university town of Leiden, where Professor van der Hoeve, the doyen of Dutch ophthalmology, together with his assistants, Drs. Copper, Binckhorst, Kok, van Wurning, and Pieck, read several papers in English and demonstrated a corneal graft operation. At Utrecht Professor Weve performed the operations of intracapsular extraction of cataract, diathermy for detached retina, and dacryocystorhinostomy, while Dr. Fischer demonstrated the use of a Goldmann contact lens for gonioscopy and showed the museum treasures. At Gröningen the emeritus professor, Dr. Rochat, demonstrated his refractometer; Professor Dekking showed a film of a cyclodialysis operation and demonstrated cases of retinitis pigmentosa treated by the subconjunctival implantation of placenta. At Amsterdam, Professor Hagedoorn performed two operations and demonstrated an apparatus for measuring orbital impressibility. Dr. Adema read a paper on squint, and some cases were examined showing the late result of corneal graft operations, fascia lata implants, and resection of the ciliary ganglion.

Zurich and Geneva

The tour of Switzerland was arranged by Mr. Muirhead and Mr. Nutt, of Sheffield. At Zurich Professor Amsler received the party, and lectures were given by Dr. Verrey on the findings from puncture of the anterior chamber; by Dr. Huber on fluorescein tests for investigating the blood aqueous barrier; and by Professor Amsler on keratoconus and on detachment of the retina. Practical demonstrations were given on the

subject matter of these lectures, and members of the party examined specimens in the pathological department and saw the work done in the photographic department. Further lectures were given by the Professor on his tests for macular function and his technique for corneal grafts. At Berne Professor Goldmann lectured on gonioscopy and demonstrated his subject on cases. He also showed his perimeter and adaptometer and his new red-free lamp. The Haag-Streit works were visited, and next day the Professor lectured again, this time on the slit-lamp examination of the fundus with a contact glass and on the location of non-magnetic intraocular foreign bodies.

At Geneva Professor Franceschetti lectured on keratoplasty, and the party was divided into groups to watch operations and demonstrations. On the following day the Professor and his staff performed further operations, corneal grafting and intracapsular extractions, while Professor de Watteville, director of the gynaecological and obstetrical clinic of the University, lectured on "Some principles underlying dosage of sex hormones." The final lecture and demonstrations were presented by Dr. Bamatter, consultant paediatrician of the clinic, the title of his lecture being "Clinical and experimental researches on toxoplasmosis."

The journey to Paris was organized by R. J. Buxton. At the Hôpital XV–XX, Dr. Schiff-Wertheimer, Dr. Dollfuss, and others gave a clinical demonstration, and later performed ophthalmic operations. Dr. Hartmann at the Hôpital Lariboisière presented an interesting demonstration and later showed his technique of intracapsular cataract extraction. Dr. Monbrun showed cases of tuberculous choroiditis treated by streptomycin; Dr. Favory and Dr. Mérigot de Treigny demonstrated ophthalmic operations. A tour of the largest dermatological museum in the world was made and a case of leprosy of the eyes shown. A corneal graft operation was performed at another hospital.

THE NEW HEALTH SERVICES: ADMINISTRATIVE PROBLEMS

PUBLIC HEALTH CONGRESS

A Public Health and Municipal Engineering Congress was held during the third week of November at Olympia. Sessions were arranged under the auspices of the Institute of Hospital Administrators, the National Housing and Town Planning Council, the Women's Public Health Officers Association, the Board of Control, and other bodies. Most of the discussions bore upon problems of administration under the new National Health Service.

The Service Developing

The Congress was opened on Nov. 15 by Mr. JOHN EDWARDS, Parliamentary Secretary to the Ministry of Health, who said that the popularity of the National Health Service had led many to suggest that it was overloaded and even in danger of breakdown. "Nothing could be further from the truth. Certainly there have been cases, as the Minister said recently, where frivolous and unnecessary use of the Service has been made. But overall its working has been amazingly smooth, and much according to our hopes and expectations." Mr. Edwards mentioned some of the tasks which confronted the Ministry of Health before and shortly after July 5, 1948. He said that 18,165 doctors out of 21,000 were now co-operating in the Service in England and Wales; 8,519 dentists out of 10,000; 5,000 ophthalmic and dispensing opticians; and 14,000 chemists. There were over 40,000,000 people on doctors' lists. Prescriptions were being dispensed at the rate of over 140,000 a year (about the rate expected); about 1,700,000 people had already had dental treatment, and about 1,500,000 people had been supplied with spectacles.

Communal Health Facilities

In a paper on communal health facilities on housing estates Mr. A. R. KERRELL-VAUGHAN gave information concerning facilities provided or projected on housing estates in various cities. In Birmingham the intention was to establish a health centre under the National Health Service Act in each neighbourhood unit or pair of units, but this policy was not capable of immediate or very early fruition. In Cardiff on each of four new housing estates there was to be a clinic or health centre at a possible cost in each case of £150,000, but here again financial stringency and difficulties concerning labour and materials prevented early materialization of the scheme. At Bristol it was proposed to divide the city into neighbourhood units of about 10,000 population, and communal health facilities were included in the basic planning of all the new housing estates. In Glasgow, in all the housing estates planned by the Corporation, provision was made for a community centre where accommodation would be available for local health authority services. At Swansea, on an estate comprising 3,500 houses, there was to be a centre with four rooms for doctors' use and two for dental services.

A Manchester councillor who took part in the discussion said that in his city the plan was to have 36 health centres and about 75 subsidiary centres. He pleaded for prefabricated construction, so that in ten years' time, if the needs of the locality have altered, it will be easy to replace the health centres. The chief demand made in the discussion was for houses to be allocated to district nurses and midwives on the new estates. Mobile health centres in rural districts were also suggested.

Hospitals under the New Scheme

Hospital administration in the National Health Service was a subject introduced by Mr. GEORGE WATTS, secretary of the Oxford regional hospital board. He described regional hospital boards and hospital management committees as an example of real partnership, each partner having fairly well defined spheres of activity but free to look to each other for help and guidance. As this service was likely to cost £150,000,000 per annum there was bound to be very strict central control, and the problem was to reconcile such control with local initiative in the regions. At present those concerned were coping day by day with a vast volume of regulations, directives, and memoranda from the Ministry. Nevertheless, a definite pattern was emerging. The Ministry was telling the regions what they must or might do, and leaving them fairly free within certain limits in the way they did it. Mr. Watts asked how far hospital management committees should be left free to carry out certain functions, and how far regional board activities should extend into the field of management. If the regional board decided to delegate the maximum amount of work to management committees it must be even more careful in the selection of such committees. In the Oxford region the management committees were settling down, and the difficulty appeared to be not to get them to work but to prevent them from running away with the bit between their teeth.

Many of those interested in the organization of the hospital service felt that the dichotomy between teaching and non-teaching hospitals was a great mistake. In the great London teaching hospitals there was probably a case for special treatment, but everywhere else the separation was a major blunder and would have to be rectified sooner or later. In the Oxford region the medical advisory committee which the board had appointed, and which included some of the most eminent specialists in the region with a leavening of other experienced persons such as general practitioners, had appointed 14 sub-committees to deal with the different branches of medicine, and this enabled the board to have direct access to the collective wisdom and experience of some 150 specialists and others in the region. It had also given the medical men concerned a real sense of partnership with the board.

Organization of Psychiatric Services

The prospective mental health services under the new Act were outlined by Dr. W. REES THOMAS. It appeared to him that the arrangements for in-patients would be somewhat as follows. Beds would be provided in general hospitals for patients of all kinds who showed no behaviour difficulties and were not otherwise unsuitable. Teaching psychiatric units

would be set up in university centres and would include research departments. Voluntary, temporary, or certified patients would be received in mental hospitals, the average number of beds needed being from 3.5 to 4 per thousand of population. Centres might be established for the treatment of patients suffering from neurotic illnesses; they would be staffed primarily by psychiatrists who would work in conjunction with consultants on the physical side of medicine. Buildings would be set aside for the treatment of old people suffering from the degenerative processes of later life. If existing observation wards in public hospitals were to continue in use, they should be staffed and equipped as hospitals or psychiatric clinics able to provide immediate skilled treatment. Beds required in institutions for defectives would probably be 2 per thousand of population. Out-patient departments should be established in general hospitals or psychiatric clinics; mental hospitals were generally unsuitable for this purpose. Separate and special arrangements were required for children needing in-patient treatment. Dr. Thomas added that the time when psychiatrists existed only in mental hospitals was long past. He hoped they were on the eve of a new era in which all the medical and social staff of the local authority or of the social agency would be trained to work for mental health.

Homes for the Old

At a special session arranged by the National Corporation for the Care of Old People Sir ERNEST ROCK CARLING described this problem, drawing upon the Rowntree and Sheldon reports and the report of the B.M.A. Committee on the Care and Treatment of the Elderly and Infirm. He said that in 1945, out of the 12,200,000 houses in England and Wales, two million were occupied entirely by persons aged 65 or over. Between six and seven million persons in this country were of pensionable age, and the proportion was rapidly increasing. Although the National Health Service was not directly concerned with the housing of those not in need of hospital treatment, it had a direct interest in the provision made for them. Considerable numbers of beds were filled and the time of many nurses was taken up by people who could be better provided for outside hospital. Geriatric units, if given comparable status to that of paediatric units and charged with continued care of incurable patients discharged to small specialized annexes, would also relieve the severe pressure on beds for acute illness. In time they would eliminate the need for long-continued bed rest in a great number of cases so treated to-day.

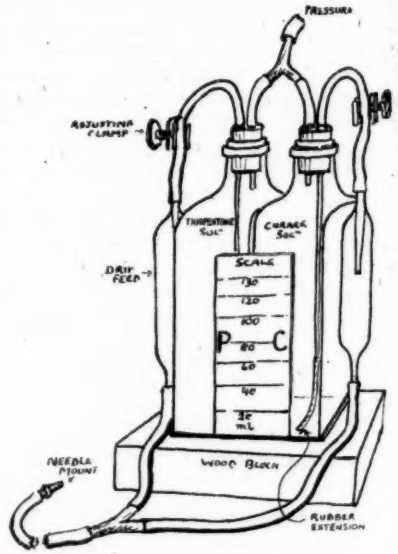
Sir Ernest Rock Carling went on to instance the several different types of hostel and home necessary to meet the phases of ageing and to suit the difference in the educational and nurtural background of the elderly. Speaking of the lowest income groups, he said that not many people even now knew the conditions in which the aged had in the recent past dragged out their miserable existence, but the sad story had come to light, and already, after less than a decade, there were very few really black spots left. The task immediately ahead was still further to improve a discreditable state of affairs, but the major problem was to prevent its persistence or recurrence; that was in the hands of the local authorities, who had to provide dwellings suited to the physical state and in accordance with the social habit of one-seventh of the population.

"On July 1, 1947, I began a new and in all probability the last period of my life." In these words Dr. Henry E. Sigerist opens his report to the Yale University School of Medicine; it is reprinted in the "Report of the Historical Library, 1947–8." Appointed Research Associate in the History of Medicine at Yale University, he is now living at Pura, a village ten miles from Lugano, in Switzerland. He had 180 boxes of books shipped across the Atlantic, and in addition he collected "dozens of large boxes" stored at Basle since 1932, when he went to America. He has now nearly finished three of the four sections that constitute Volume 1 of his *History of Medicine*. This volume is on medicine in prehistoric times and in ancient Egypt and Mesopotamia, with a chapter on the medicine of the Hebrews. The volume will include a bibliography of palaeopathology after 1930 and a critical bibliography of histories of medicine. He plans to discuss in Volume 2 the initial phases of medicine in India and China.

Preparations and Appliances

ANAESTHETIC APPARATUS FOR CONTINUOUS ADMINISTRATION OF THIOPENTONE AND CURARE SOLUTIONS

Dr. R. ATWOOD BEAVER, senior anaesthetist, London Chest Hospital, writes: For some time a routine method of anaesthesia for thoracotomy has been the administration of thiopentone and curare via the blood drip. The usual procedure is to puncture the rubber tube with a hypodermic needle, giving divided doses as required. It has been felt that this somewhat unaesthetic procedure results in extremely uneven depth and that continuous administration is preferable.



The simple machine here illustrated has accordingly been developed. It can be made most satisfactorily from the standard blood-bottles, but a neater machine consists of two bottles with flat sides as shown. Pressure is supplied by a hand bulb or, better, from an oxygen cylinder with valve reducing the pressure to 5 lb. (2.27 kg.) or less. This does not affect the solutions. The mixed fluid is supplied in the ordinary way via a needle strapped into the rubber blood-drip tube or on occasion by direct insertion into a vein. The strength of the solutions is such that they can easily be regulated within the desired limits by the pinch-screws. Typical figures are: curare, 10 mg. per 100 ml.; thiopentone, 5%. In these dilutions there is no precipitation on mixture. Certain desiderata must, however, be observed.

1. The pressure must be sufficient to overcome that of the "head" of blood from the drip-bottle.

2. To this end the area of the rubber stoppers must not be too large or they will blow out.

3. The delivery tubes inside the bottles should be prolonged to the bottom by rubber extensions.

4. To avoid any risk of air embolism Macintosh-type drips should be used, but for reasons of clarity they have been omitted from the illustration. If ordinary drips are used the level of fluid should not be allowed to fall below ¾ in. (18.75 mm.) of the bottom of the bottles.

The procedure is to induce with the usual concentrated solutions by syringe and, after the preliminaries have been completed, to continue by adjusting the drips as required.

For other operations varying solutions may be given, such as thiopentone solution and saline, thiopentone solution and adrenaline solution, saline and blood.

My thanks are due to Mr. T. Holmes Sellors, on whose cases the apparatus was developed, and to Dr. Roger Wright for his assistance and suggestions.

Reports of Societies

BRITISH ORTHOPAEDIC ASSOCIATION

ANNUAL MEETING

The annual meeting of the British Orthopaedic Association was held in Belfast from Oct. 21 to 23 under the presidency of Mr. S. A. S. MALKIN.

Painful Shoulder

Only pain of intrinsic origin was considered. In an introduction Professor GEORGE PERKINS (London) referred to invariable complete recovery in capsulitis, a generalization denied by subsequent speakers. Mr. V. H. ELLIS (London) found it difficult to fit such conditions as the stiff shoulder complicating coronary disease into a simple classification of extrinsic and intrinsic causes. He described the production of supraspinatus injuries, and pointed out that loss of power in the supraspinatus might be reflex and recover quickly or might be the consequence of a complete tear demonstrable by arthrography. Removal of the acromion facilitated suture of the supraspinatus and hastened recovery. Mr. J. TULLOCH BROWN (Killearn) had found that in severe cases of the supraspinatus syndrome procaine infiltration was useful in distinguishing patients with loss of movement from spasm, requiring conservative treatment in the first instance, from those in whom structural changes demanded operation.

Mr. R. J. W. WITHERS (Belfast) had found 61 cases of capsulitis in 100 cases of intrinsic pain in the shoulder. Two stages might be distinguished : "irritative" capsulitis in which the stiffness was due to spasm and disappeared under anaesthesia, and "adhesive" capsulitis in which stiffness persisted under anaesthesia. The former was treated by rest in a sling, followed by active exercises at the end of about six weeks. "Adhesive" capsulitis demanded primary manipulation followed by exercises. Mr. W. C. SOMERVILLE-LARGE (Dublin) emphasized the value of anaesthesia in distinguishing between muscle spasm and structural change as the cause of limitation of movement. Mr. STEWART H. HARRISON (Birmingham) had found radiological changes in 30% of patients with pain and stiffness of the shoulder following injury and had found that such cases did not completely recover. Mr. F. A. SIMMONDS (Pyrford) had found in a three-year follow-up that some patients still had slight pain, weakness, and stiffness. Biopsy in the active stage had revealed degenerative changes in the tendinous cuff with a chronic inflammatory reaction but no intra-articular change. The use of a sling and the performance of exercises within the painless range were useful, but he agreed with others that heat was of doubtful value.

Mr. J. R. ARMSTRONG (London) advised excision of the acromion in those patients with the supraspinatus syndrome who did not recover spontaneously. He had found a variety of lesions with similar symptoms : supraspinatus tendinitis, partial and complete supraspinatus tears, calcification in the tendon, and subdeltoid bursitis. Mr. G. BLUNDELL JONES (Exeter) referred to acute cases of supraspinatus calcification with sudden pyrexial onset, short course, and early dispersal of the calcium deposit. Mr. W. E. TUCKER (London) mentioned focal sepsis and gout as causes of shoulder pain and agreed upon the importance of rest in the acute stage.

Mr. C. K. WARRICK (Newcastle-upon-Tyne) then described three cases of posterior dislocation of the shoulder, and advocated that, unless stereoscopic views could be taken and inspected, the ordinary antero-posterior view should be supplemented by a vertical view with the *x*-ray tube in the axilla, or a vertical view with a curved cassette in the axilla, or a profile scapular view.

Operations on the Hip and Femur

Mr. J. S. BATCHELOR (London) described removal of the femoral head and neck from 50 hips in 44 patients with the object of promoting mobility. In 32 a sub-trochanteric osteotomy also was performed for the promotion of stability. This might be undertaken at the primary operation, with plating of the fragments; or three to five weeks later through a separate approach, a tongue being cut in the distal fragment to ensure its engaging with the proximal. After a period of light skeletal traction walking was resumed after eight to ten weeks. Operation has been undertaken for osteoarthritis, ankylosing spondylitis, fracture-dislocation, ununited fracture of the femoral neck, ankylosis from old acute arthritis, and chronic suppurative arthritis. The results were : satisfactory 39 ; unsatisfactory 10 ; death 1. Unsatisfactory results included instability (3), pain (3), lack of co-operation (2), restriction of movement (1), and non-union of osteotomy (1).

Mr. NOEL J. SMITH (Peterborough) showed a femoral head eight weeks after the performance of a vitallium cup arthroplasty for osteoarthritis. The denuded surface had become covered with smooth fibrous tissue and fibro-cartilage. Mr. H. A. BRITTAIN showed a film of his operation of ischio-femoral arthrodesis. Mr. H. H. LANGSTON (Alton) had performed 30 of these operations, without sciatic nerve injury but with failed union in 5, perforation of the obturator foramen with the graft in 2, and sequestration of the graft in 1. Mr. W. B. FOLEY (Oxford) advocated open operation through a posterior incision reflecting the gluteus maximus upwards and inwards; fusion had taken place in 16 out of 17 cases. Mr. G. K. MCKEE (Norwich) gave a preliminary communication describing and illustrating the use of a lag screw in combination with cancellous grafting in ilio-femoral arthrodesis. Mr. JOHN CHARNLEY (Manchester) gave an account of preliminary and unsuccessful attempts at arthrodesis by impaction of the tapered femoral head into a hole in the acetabular floor.

The Hand

Mr. W. H. GERVIS (Tunbridge Wells) reported 18 cases of arthritis of the first metacarpo-carpal joint treated by excision of the trapezium, with good results in all cases of osteoarthritis but with poor results in two cases of rheumatoid arthritis. Mr. A. DORNAN (Sheffield) had found that conservative treatment gave good results in most cases of Kienböck's disease; so did excision of the lunate (semilunar) bone, even after failure of conservative treatment. Mr. GORONWY E. THOMAS (Liverpool) had investigated the results of treatment for non-union of the carpal scaphoid carried out three years before. The 28 treated conservatively had done very much better on the whole than 52 patients treated operatively, of whom only 7 were able to return to heavy work. The series were not strictly comparable, however. Backward subluxation indicated a bad prognosis.

A number of other papers were read and Mr. NORMAN CAPENER (Exeter) showed a "lively" splint to allow supported movement of the abducted arms in convalescence from infantile paralysis.

SOUTH-WESTERN REGION SOCIETY OF ANAESTHETISTS

The second annual general meeting of the society was held at Bristol on Oct. 29 and 30. Fifty-seven members were present, many of them accompanied by their wives. The chief guest was Dr. John Gillies, of Edinburgh, President of the Association of Anaesthetists of Great Britain and Ireland, who gave an address on "Spinal Analgesia—its Present Status." Other papers were read by Mr. Geoffrey FitzGibbon on "Problems of Anaesthesia for Plastic Surgery," by Dr. T. B. P. Wilton on "Anaesthesia for Thoracoplasty," and by Dr. R. F. Woolmer on "The Explosion Risk." Practical demonstrations were also given at the Bristol Royal Hospital and at the Thoracic Unit, Frenchay. An attractive social programme was arranged for the wives of members.

The Chelsea Clinical Society's second dinner meeting of the session was held on Nov. 9 at the South Kensington Hotel, London, S.W.7, with the president, Mr. Nils Eckhoff, in the chair. A paper was given by Mr. John Hanby on "The Value of Chiropody in Foot Disabilities," and this stimulated an excellent discussion.

Correspondence

Inactivation of Viruses by Heat

SIR,—The important communication of Drs. H. Malmros, O. Wilander, and B. Herner on inoculation hepatitis (Nov. 27, p. 936) raises the whole problem of the inactivation of viruses by heat. They finally suggest the use of dry heating for routine sterilization of syringes, etc. May I be permitted to submit the result of an experiment in which the effect of moist and dry heating was compared in the case of the virus of vaccinia? One of our sisters at St. Bartholomew's had taken service with a mission in Central Africa, and on her leave she sought me out for help about vaccine lymph. The chief disease that they feared at her station was smallpox, which spread there like wildfire among the natives when introduced, and three times over they had found that vaccine lymph coming up from the coast had become inactivated by the heat during its transit.

I was working on vaccinia at the time, and tested the effect of heat on the same virus when suspended in broth in the usual way and when the same specimen had been dried in a desiccator and, after being powdered, resuspended in similar broth. The results were striking. When moist the virus was inactivated completely by exposure for 30 minutes to 65° C., but when dried it not only withstood that amount of heating but even half an hour at 70° C. failed to inactivate it; it was not till the same exposure to 80° C. was used that it became inert. Before she left I sent the sister some of this dried vaccinia virus, but I never heard if she got it or not.

The great merit of half an hour's exposure to 65° C. as a routine is that it can be used easily by having an ordinary covered vaccine-bath such as most laboratories possess. Moreover, should any tubercle bacilli be present they are destroyed, as I have verified again and again by the guinea-pig test with glands removed for biopsy.—I am, etc.,

Molesey, Surrey. M. H. GORDON.

The M'Naghten Rules

SIR,—I was impressed by the wisdom of your brief comments on the M'Naghten rules (Nov. 13, p. 882), and am sorry that Dr. Clifford Allen (Nov. 27, p. 955) protests at your "complacent attitude" in a letter which unfortunately is far from showing any real understanding of the matter and its difficulties. His complaint that after the opinion of a competent psychiatrist the issue (of the accused's sanity or insanity) is placed in doubt by the prison doctor's contrary opinion shows that he has not grasped the elementary fact that that issue, just like the issue of a prisoner's guilt or innocence, is a legal problem, not a medical one, and that "Law from Harley Street" is a thing that very rightly has never been, and will never be, tolerated in this country.

Of course the issue is in doubt. That is why it is tried, and, fortunately for the interests of justice (and of mercy), the law does not accept the *ipse dixit* of any psychiatrist as a substitute for such trial. I hasten to say that I, for one, should hesitate a very long time before certifying a patient who "stated that his father had been insane and that he himself had impulses to murder children" if that were all I knew about him, and I should greatly like to see the certificate which anyone who attempted the task would produce.

Dr. Allen reflects—unfairly and inaccurately in my view—upon the training and experience of prison doctors, and proceeds to commit himself to the principle that if a man is medically certifiable he is legally irresponsible. How such a principle could conceivably be accepted by anyone who had spent even a month or two as a resident physician in a mental hospital passes my comprehension.

I have given evidence in many murder trials, in two of which the prison doctors were strongly and openly opposed to my view, but in these, as in all the others, I received not only absolute fairness but very definite assistance from the judge in my efforts to find a form of words which without sacrificing medical accuracy would express the accused's mental disorder in terms of the M'Naghten rules. I have also had the opportunity of repeated private discussion of these rules with some of the highest legal authorities in the country, and in consequence I know something of the difficulties and dangers which stand in the way of tampering with them. I am also in a position to confirm most confidently the opinion that they work well in practice and to state that Dr. Allen's outline of their working in "case after case" is a travesty of the facts.

Full discussion of this matter, which is so often and so grossly misunderstood by our profession, would be unsuitable in your correspondence columns. May I repeat once again, however, the elementary point that the function of the expert witness is to assist the court in coming to its decisions. If he is not prepared to let the court conduct its investigations in its own way and to give his evidence without protest in accordance with the rules that the law lays down, then his evidence will be largely valueless and he has no right to appear as a witness at all.—I am, etc.,

London, W.1. HENRY YELLOWLEES.

SIR,—Dr. Clifford Allen (Nov. 27, p. 955) invites the profession to agree that "if a man is medically certifiable he is legally irresponsible." It is to be hoped that this proposition will not be put forward to the legislature as the view of the medical profession, for in my opinion it is quite untrue. I am not a dyed-in-the-wool psychiatrist or psychologist, but I did spend six war years as medical officer in the mental hospital service; and that experience convinced me that a lot of nonsense is written and spoken about irresistible impulses in the insane. Such things do no doubt occur, but only in a small minority. The bulk of the certifiable insane can and do restrain dangerous impulses if they are given sufficient inducements to do so—i.e., if they are under strict, though not of course harsh or inhumane, discipline.—I am, etc.,

Tunbridge Wells, Kent. HENRY ROBINSON.

SIR,—About 20 years ago it was a common sight in general hospitals to see police officers sitting by the bedsides of patients who had cut their throats, and suicide was regarded as a crime. Since those days our attitude towards suicide has changed to such an extent that even a suicidal threat is now regarded as sufficient grounds for certification. Alternatively the person may be persuaded to enter a mental hospital as a voluntary patient. In either case the possessors of such impulses are no longer regarded as potential criminals but merely as a danger to themselves.

Perhaps in a further 20 years' time all those who have proved themselves to be a danger to others will also be allowed to live peacefully under supervision in the hospitals provided for that purpose, instead of being prematurely dispatched to another world.—I am, etc.,

Lancaster. R. PAKENHAM WALSH.

Pre-suppurative Amoebic Hepatitis

SIR,—The case reported by Mr. C. F. Critchley (Oct. 9, p. 681) again raises the question whether an amoebic liver abscess can arise in a patient who has never left this country. From a theoretical standpoint it seems possible, though recent literature contains no record of such a case. In Mr. Critchley's case such a diagnosis would have been established had *Entamoeba histolytica* been found in scrapings taken during sigmoidoscopy and from the cavity wall at operation—an examination which might profitably be performed in any liver abscess of doubtful aetiology.

Certainly the risk of developing amoebiasis in this country must be increasing with the return of Service personnel from endemic tropical and sub-tropical areas. The cyst-carrier rate in ex-Servicemen of other countries has been proved to be far higher than that of the indigenous population (5–10%)—e.g., 20% in Italians,[1] 25% in Germans,[2] and 26% in Americans.[3]

Lastly, one wonders whether the syndrome of pre-suppurative amoebic hepatitis exists in this country in ex-Servicemen and could arise *de novo* in one who had never left this country. Although based on sound pathology and long recognized by some clinicians (Brown,[4] Rogers[5]) its indeterminate features make it difficult to diagnose, impossible to prove, and in consequence many doubt its existence.

Pathologically the solitary liver abscess is preceded by a diffuse amoebic hepatitis secondary to an intestinal lesion which is usually occult. Miliary abscesses may then form in the liver and may later coalesce to form the solitary large abscess. Symptoms are vague. Patients generally feel off colour and complain of fatigue after accustomed exercise, of slight heaviness in the upper abdomen (e.g., after wearing military equipment), or of feeling less like their usual quota of alcohol. Physical findings are also vague. There may be slight tenderness on heavy percussion over the liver, tenderness of the right acromium ("the liver wing") or of the right trapezius muscle. The liver is generally not palpable, and liver-function tests, sigmoidoscopy, barium *x*-rays, and stool tests usually reveal no abnormality.

On such slender criteria sceptics may well be forgiven, and diagnoses of functional dyspepsia, hepatitis *sine* icterus, etc., are often made. If, however, such cases are given emetine they make a dramatic symptomatic recovery. This treatment has sometimes, though perhaps ill-advisedly, been given to out-patients without other treatment to which recovery might have been ascribed. Similar cases in England might well be given emetine as a therapeutic test, followed by intestinal therapy for successful cases.

Though proof of diagnosis seems impossible in most cases, perhaps the wider use of hepatic biopsy may bring such cases to light. Once diagnosed, treatment is specific and the development of a large abscess prevented. The condition probably occurs at least ten times as frequently as solitary abscess, and, if Mr. Critchley's case represents an amoebic abscess, then the possibility of pre-suppurative amoebic hepatitis must be constantly considered in patients who have never left the British Isles.—I am, etc.,

Hadley Woods, Herts. JAMES T. HAROLD.

REFERENCES

1 Horster, *Dtsch. tropenmed. Z.*, 1943, **47**, 299.
2 Angelini, G., ibid., 1943, **47**, 228.
3 Sapero, J. J., *Nav. med. Bull., Wash.*, 1939, **37**, 279.
4 *Amoebic or Tropical Dysentery*, 1910, London.
5 *Bowel Diseases of the Tropics*, 1921, London.

Treatment of the Infertile Marriage

SIR,—Mr. R. Christie Brown's paper (Nov. 13, p. 851) might encourage the general practitioner to adopt a treatment which has no proper scientific basis. We therefore wish to make a few observations. It has been left open whether his 111 cases "medically treated" were selected or non-selected ones. No patients' ages were given and, more important still, no mention was made as to how many years the patients have been trying for conception, only that all of them had been sterile for more than two years. We accept that all the patients in question had a regular 28-day menstrual cycle, a fact which in itself would not be quite usual if the cases were non-selected.

Does Mr. Christie Brown really believe that the success in 13 out of his 38 patients—i.e., 30% of the successes—who have become pregnant one month after the commencement of treatment is due to 0.6 mg. of "dienoestrol" and 10 mg. "ethisterone" taken daily for not more than 14 days? Is there any explanation why the percentage of successes decreases in the second and third months and reaches its peak six months after the beginning of treatment if, according to Mr. Christie Brown, no other than medical treatment alone was given? Or do we take it that the comparatively high figure of successes after six months is due to the fact that investigations were undertaken after three months as well as the medical treatment?

We all know that not all endometria show the same degree of preparation and that it is fallacious to base an opinion on one finding only. There is no record in Mr. Christie Brown's article that endometrial biopsies were performed, so that it is difficult to say what percentage of the 38% successful women suffered from incomplete development of the secretory phase. It is difficult to conceive that such a small dose of progesterone taken by mouth can in one, two, or three cycles influence a poorly functioning endometrium.

Oestrone as a sensitizing hormone in the first half of the cycle followed by progesterone alone or in conjunction with small doses of oestrone has been given for a long time by many of us with, unfortunately, disappointing results. Experience has shown that delay in onset of the period could be quite considerable, even sufficient to suggest a pseudopregnancy, only to be excluded if a temperature record has been kept.

With regard to the results of repeated miscarriages treated in the same way we should like to compare the figures of Malpas[1] with those given by Mr. Christie Brown:

	Malpas	Christie Brown
(1) 2 successive abortions, spontaneous cure rate ..	78·4%	57·8%
(2) 3 " " " " " ..	62%	50%
(3) 4 " " " " " ..	27%	—
(4) 5 " " " " " ..	6%	25%

We do not consider that the psychological effect on the patient is good in continuing a treatment for six months which may be entirely misdirected should the Fallopian tubes ultimately be found to be non-patent. There may be so great a variation in any series of cases conducted by one individual in different years (42% successful pregnancies in one year, 22% in another, as analysed by one of us) that a much larger series of cases would be required to be treated before true evaluation of the treatment can be estimated.—We are, etc.,

M. MOORE WHITE.
E. FRIEDMANN.

London, W.C.1.

REFERENCE

1 *J. Obstet. Gynaec. Brit. Emp.*, 1938, **45**, 932.

Herpes Zoster Treated by Anthisan

SIR,—As any severe case of herpes zoster is usually refractory to all treatment and the pain may become well-nigh intolerable I wish to report a case that responded immediately. As this disease is due to a virus with pathological inflammation of the dorsal root ganglia or Gasserian ganglion, and as it is the sensory analogue to anterior poliomyelitis and has the same type of lesions in the nervous system and similar cerebrospinal-fluid changes, the same treatment may be worthy of trial in anterior poliomyelitis.

The patient was a well-built, very active man of 64 years who presented himself for treatment on account of severe neuralgia affecting the frontal area of the head, the lower jaw, and the occiput on the right side. Very small vesicles were discernible over the supra-orbital area only. An anaesthetic local application and analgesics were given. The patient was not seen for two days after the first consultation, when he was again seen on account of very severe supra-orbital pain which had prevented him from resting or sleeping for two nights and days. There were large pustules and vesicles corresponding to the supratrochlear and supra-orbital nerves. Oedema was fairly intense and the right eye was closed. There was no involvement of the cornea.

On account of the severe pain not being relieved by the usual analgesics he was given pethidine four-hourly. This gave no relief, and for the next 24 hours he was still in very acute pain and stated that if he had to bear any more he would become distracted. It seemed that he would have to be given morphine. However, it was decided in the afternoon at 3 p.m. to start him on "anthisan," 1 tablet of 0.1 g. every four hours. Within one hour the pain had lessened, and after the second tablet it had disappeared. Tablets were continued at four-hourly intervals, and he slept all night and all next day, having no pain at all. The oedema rapidly subsided and the pustules and vesicles rapidly healed.

In many cases of herpes zoster pain persists for weeks and even months despite every form of treatment. The above treatment was so immediately beneficial and so dramatic that there is no doubt that anthisan was a specific agent here. "Anthisan" (pyranisamine maleate) is an active antihistaminic agent and has been shown experimentally to possess considerable local analgesic activity. It is stated to be more likely to prove effective in the superficial forms of allergic disorders and in cases uncomplicated by secondary infections and structural changes. In the above case benefit was apparently not due to lessening of oedema and inflammation alone, as the oedema and inflammation took 36 hours to subside completely after the first administration. There was probably a specific action on the nervous system and/or the virus.—I am, etc.,

Birmingham. MAX HONIGSBERGER.

Barbiturate Poisoning and Picrotoxin

SIR,—The interesting medical memorandum by Drs. R. W. Bazeley and P. H. Garrard (Nov. 27, p. 943) shows again the value of picrotoxin in the treatment of barbiturate poisoning. I agree with the authors that only large doses of picrotoxin are of any use, and this fact merits general recognition. With careful observation of the patient picrotoxin overdosage is a remote theoretical danger, the more so as patients in barbiturate

coma can tolerate enormous amounts of picrotoxin. I have used the drug in all cases of coma due to poisoning with different members of the barbiturate group since early in 1946 and have had only one fatality; this was in the case of a woman who was unconscious for longer than 24 hours before starting treatment.

For the drug to have effect it should be given at regular intervals, first by the intravenous route and then by intramuscular injections; it must be persevered with until the first signs of recovery are apparent. Relapses are an indication for a renewal of picrotoxin injections. Nauth Misir[1] treated successfully two cases of barbiturate poisoning with 1,745 mg. and 1,024 mg. of picrotoxin respectively. However, a total dosage not exceeding 500 mg. will be found sufficient in most cases of barbiturate poisoning of marked severity. My own procedure follows the general lines as pointed out by Nauth Misir: the first intravenous injection may range from 6 to 30 mg. of picrotoxin, and this is followed 15 minutes later by either more intravenous injections of doses of 6 mg. or similar amounts given intramuscularly every 15 or 20 minutes. This treatment is continued day and night until the patient shows signs of coming round. In an article on the subject I have also reported a case of deep coma due to paraldehyde poisoning which responded in a dramatic way to picrotoxin treatment.[2]—I am, etc.,

London, W.10. A. I. SUCHETT-KAYE.

REFERENCES

1 *Lancet*, 1946, **2**, 381.
2 *Pr. méd.*; 1948, **56**, 495.

Prescription of Barbiturates

SIR,—"These tablets are dangerous." This phrase is now so commonplace as a precedent to the News that it appears past comment. Are we right, however, in prescribing in such large quantities a depressing and wit-dulling drug such as "feenobarb" instead of the time-honoured aspirin, plain or coloured?

We rightly condemned our Victorian parents for using soothing syrup containing opium to quieten the squalling infant. I am informed by a pharmacist whom I know well that phenobarbitone is now commonly prescribed in doses of ¼–½ gr. (16–32 mg.) two or three times a day to infants a few months old, and that prescriptions for adults of large quantities of this barbiturate are so numerous as to suggest that half the population is constantly under the influence. Is it not time, Sir, to reconsider how and when to use these cerebral depressants and to realize that they must be doing considerable harm to the nation?—I am, etc.,

London, W.1. T. PEARSE WILLIAMS.

Diagnosis of Tuberculous Meningitis

SIR,—The introduction of streptomycin in the treatment of tuberculous meningitis renders the early and correct diagnosis of this disease of even greater importance than in the past. I would therefore like to draw attention to the significance of the glucose content of the cerebrospinal fluid in this condition.

The fact that a low value is found is of course well known, but the highly specific nature of this finding seems to have escaped attention. I have notes of 65 cases of tuberculous meningitis examined in the laboratory of the Belfast City Hospital, in all of which tubercle bacilli were demonstrated in the cerebrospinal fluid and in which the cells, protein, glucose, and chloride content were estimated. On classifying these cases the following figures were obtained:

Glucose in mg. per 100 ml.	*Number of Cases*
40–50	2
30–40	10
20–30	18
under 20	35

It will be seen that in only 2 out of 65 cases was the glucose value above 40 mg. per 100 ml., in 53 it was under 30 mg. per 100 ml., and many of the cases described as "under 20 mg." showed the merest trace of glucose. I would also point out that this fall in glucose is an *early* sign; sometimes 2 or 3 spinal punctures were necessary to demonstrate tubercle bacilli, but the glucose was always low from the first, though falling still lower as the case progressed. It is well known that in other cases of non-purulent meningitis—e.g., poliomyelitis, benign lymphocytic meningitis, cerebrospinal syphilis, etc.—the glucose content of the fluid is normal, a fact which has been repeatedly confirmed in this laboratory. The chloride content, though often lowered, does not show the same invariable fall, and is not reliable in the diagnosis of tuberculous meningitis.

I am now so convinced of the specific value of a low glucose content that I have no hesitation in basing a diagnosis on this fact alone in the presence of a pleocytosis of the lymphocytic type. If the value is below 40 mg. per 100 ml. the diagnosis is highly probable; if below 30 mg. per 100 ml. it is certain. On the other hand, a value over 50 mg. per 100 ml. practically excludes the disease. I therefore put forward a plea for the more general adoption of this test in the diagnosis of tuberculous meningitis.—I am, etc.,

Belfast. J. T. LEWIS.

Intravenous Procaine in Transfusion

SIR,—With reference to the medical memorandum on this subject by Drs. G. S. W. Organe and C. F. Scurr (Oct. 30, p. 787) I found during the war that venous spasm, indicating fairly severe shock, was quickly overcome by rapid transfusion of a liberal volume of blood or plasma, using positive pressure. Other important points to be noted are:

(1) Obstruction to the flow of blood into a vein is usually due to blood clot in the leads or needle of the blood-giving set, and is relieved by replacing one or both of these.

(2) Vasoconstriction of the vessels supplying the vital medullary centres—the apparent cause of shock—may not necessarily be overcome by replacement of a volume of protein fluid equal to the volume of blood lost; this explains why transfusion of larger volumes may be necessary.

(3) This vasoconstriction is mechanically, but entirely temporarily, overcome by lowering the head end of the patient. Therefore a case of shock that is apparently fully resuscitated in the head-low position will often require transfusion of several pints more when raised to the horizontal position.

(4) Shock is a major cause of death in abdominal wounds and operations, and since the head-low position is found to be effective in the treatment of shock the use of Fowler's position post-operatively must cause a multitude of deaths. Penicillin and sulphonamides now being available to prevent peritoneal infections, it remains for some courageous surgeon to treat his abdominal operation cases rationally in the horizontal position post-operatively, having given at the same time liberal transfusion—i.e., six to twelve pints (3.4–6.8 litres)—of protein fluid.

(5) If this is done it may be necessary to give intravenous saline post-operatively only when the gut has to be kept at rest.

(6) Vigilant observation of the respiration rate during transfusion is necessary in abdominal cases to prevent pulmonary oedema, as, in marked contrast to limb-wound cases, the pulse may remain poor after adequate transfusion or even when pulmonary oedema has occurred.

(7) Liberal transfusion so improves a patient's morale that genuine neurotics might benefit remarkably by small transfusions (perhaps three pints) of protein fluid.

—I am, etc.,

London, W.14. A. D. MILNE.

Justifiable Laminectomy

SIR,—I was interested in Dr. J. C. W. Hopkyns's memorandum entitled "An Unusual Trophic Ulcer" (Nov. 20, p. 905), but a little surprised at his conclusions. Having practically proved that his patient has a prolapsed disk at the lower end of his spine causing a trophic ulcer in his foot, he proposes to leave the *fons et origo malorum* alone and merely "intensify the local treatment to the ulcer." This ulcer will almost certainly get worse, as the cause of it has not been removed, and a man of 29 is being condemned to numbness of the heel and thigh and, at the very least, a progressive ulceration for the remainder of his life. From my experience as an ordinary G.P. I would make a guess that within a year or so other and far more serious neurological symptoms will occur, possibly, if bladder complications supervene, resulting in the death of the patient. May I take two illustrations from my own practice?

1. Foundry worker, aged now about 44, discharged from the Services in 1942 for sciatica and lumbago, probably caused by a prolapsed spinal disk. I could get no orthopaedist to tackle his spine,

but he got great relief from 6 months in a plaster jacket. As soon as this was taken off his pains came back. Eventually a skilled orthopaedist decided to deal with the cause, and about 9 months ago he did a laminectomy and removed a prolapsed disk. Since then the patient has had no pain and has gone back to work.

2. Farm labourer, aged about 40. In October, 1942, he developed slight loss of power in both legs, a symptom which increased rapidly. There was weakness of the left hip and knee, loss of left lower abdominal reflexes, and flexor plantars. W.R. and Kahn were negative. He was then discharged and sent home no better. In April, 1943, I sent him to London, where he was thoroughly tested in two famous neurological centres. "Pressure paraplegia, due to either an intramedullary or extramedullary tumour" was the verdict. In favour of the former was the Brown-Séquard syndrome of the stronger right leg being the more analgesic. The upper limit of the analgesia faded away gradually from D.12 to D.10. C.S.F. in April, 1943: pressure 100, jumping up briskly on jugular compression, thus excluding spinal block (Queckenstedt); W.R. negative; total proteins 35 mg. per 100 ml. Histamine test meal showed plenty of free acid, thus excluding P.A. Lipiodol injection high up in spine showed on *x*-ray no evidence of spinal block. Everything being negative, he was sent back to me again with instructions to "carry on with his work as well as he could." By now he was staggering along on two sticks.

In September, 1943, I sent him to another hospital, as I felt sure, though entirely ignorant, that a laminectomy was the answer. His C.S.F. then showed 55 mg. of protein. It was proved later that there was, in fact, spinal block in this case, though manometry did not show it. Increase of C.S.F. protein below the level of the block, or cord compression, is part of Froin's syndrome and is probably due to compression of the spinal veins. As a result the pressure within these veins rises and consequently blood corpuscles and plasma containing much protein exude. By July, 1944, the plantar reflexes were extensor, but Queckenstedt's test was still negative and there was no evidence of block. Dorsal fluid showed cells 9 per ml. and protein 30 mg. per 100 ml. But in the lumbar region the cells were 1,500 per ml. and the protein 225 mg. per 100 ml. At long last, in July, 1944, a laminectomy was done, and between D.11 and D.12 a large, hard, prolapsed, calcified intravertebral disk was found and removed. The cord below it was grossly atrophied for ¾ in. and displaced to the right. But it was too late. On July 15, 1944, he had a violent haematuria and collapsed and died the next day. Post-mortem examination confirmed the operative findings and showed a gangrenous cystitis.

There is no doubt in my mind that if a laminectomy had been done two years previously the life of this hard-working, skilled, and conscientious farm expert could have been saved. The ordinary G.P. is left wondering: (1) What are the risks of laminectomy? Surely they could not include the death of the patient if the spine was found to be normal? (2) Why do not physicians, if paralysis increases and the patient's condition deteriorates, in spite of all negative spinal findings insist on laminectomies?—I am, etc.,

Stowmarket, Suffolk. H. S. GASKELL.

Peptic Ulcer in Pregnancy

SIR,—The excessive rarity of symptoms of peptic ulceration during pregnancy has been stressed by all authorities, and the interesting case reported by James (1948) is therefore a warning that one should be on the look-out for such cases. The fact that, though rare, the disease is often fatal is all the more reason to pay serious heed to continued symptoms of dyspepsia during pregnancy, especially where the patient is a known sufferer from ulceration of the stomach or duodenum.

Bralow, Scheinberg, and Necheles (1948) have just recorded four more cases from Chicago. Perhaps only one of these could strictly be reckoned a complication of pregnancy in that the patient, who was known to have had a duodenal ulcer eight years previously, suffered from epigastric pains during the whole term of her pregnancy. Her symptoms entirely disappeared as soon as the pregnancy terminated, nor had they reappeared since, even during a second pregnancy four years later.

There are three main groups of theories to account for the rarity of peptic ulcer in pregnancy—the mechanical, the chemical, and the hormonal. As already mentioned by James, Hurst was the first to suggest that the rising uterus supported a lax stomach and so induced a better blood supply in the lesser curvature. Both in James's case as well as in one cited by Mulsow and Brown (1936) the major accidents took place at a time when the stomach could not have been lifted much higher—in the later weeks of pregnancy.

Balint (1927) first suggested a general tendency towards increased alkalinity in tissue fluids during pregnancy, and other observers have confirmed that with increased alkalinity there is found a hypo- or even achlorhydria, especially in the first six months of pregnancy; thereafter the acid values began to rise towards normality and might even reach supernormal figures in the puerperium in certain cases.

Crohn (1927) and others noted that peptic ulcers tend to break down in the puerperium. Winkelstein (1940) thought that the agent responsible for the breakdown might possibly be prolactin, the lactogenic hormone of the anterior pituitary. During gestation the formation of prolactin is inhibited by the high blood-levels of ovarian and placental hormones. He made experimental studies on animals with chemically produced peptic ulcers by treating them with the ovarian hormone theelin. The response was good and the ulcers healed within ten days. Abrahamson, Church, and Hunter (1942) treated peptic ulcers in human beings with theelin, and, while getting a slightly better immediate response as compared with a number of controls treated on routine lines, found the long-term results no better.

Of these three theories, then, that of hormonal control would appear to be the most probable. It was seen above how the mechanical theory was apparently disproved by the occurrence late in pregnancy of major complications of ulcer. The chemical theory would appear to be at fault in the following case.

CASE REPORT

There is at the moment in my wards a woman 34 years old who is suffering from a relapse of ulcer symptoms and whose barium meal three weeks ago showed the presence of a duodenal ulcer. The cause of the present relapse was sought in her personal history, and it is quite reasonably ascribed to the fact that she and her mother-in-law have to live under the same roof. From the age of 18 she had suffered from slight, vague, windy indigestion, to which she paid little heed. In 1943 she was married and later that year became pregnant.

At about the second month of pregnancy she got a bad fright. A kettle of boiling water fell over her sister's foot, the patient witnessing the accident. She has, she says, always reacted strongly to any family accident, having lost her voice on two previous occasions of mishap. On the night of this accident the patient went to bed with a pain in the epigastrium such as she had not previously felt, and she vomited. In such state she continued for the next 36 hours until the pain suddenly became intolerable, and she was admitted to this hospital as an acute abdomen. At operation a perforated peptic ulcer was found and repaired, and the patient's post-operative and subsequent gestational progress was completely uneventful.

Wild surmises of having stumbled across the first case of "psychogenic" Curling's ulcer were dispelled by the operation notes (Mr. G. W. Duncan), which revealed that not only was the ulcer prepyloric in position—incidentally the commonest position in which a simple benign ulcer perforates—but it appeared from the surrounding induration to be chronic.

Another case was that of a woman of 41 admitted on Aug. 25 suffering from severe hypochromic anaemia. She gave a history of intermittent dyspepsia since the age of 24, when she had a severe haematemesis and was ill for the next eighteen months. She had no further trouble until she became pregnant at the age of 28, when she vomited blood on several occasions during her pregnancy and had ulcer pain for a number of weeks. The pregnancy came to a successful conclusion and was followed by a slow return to normal health. For the next seven years the patient was symptom free until, in 1943, she was admitted to Hillingdon Hospital with a recurrence of ulcer pain and haematemesis. Barium meal showed a duodenal ulcer, and six months later, on re-*x*-ray, a small ulcer was still seen. In 1944 she became pregnant again and once more ulcer pain and haematemesis recurred. The pregnancy terminated successfully. Since 1944, every six months there have been recurrences of pain and haematemesis. During her present admission she had irregular pain and some tenderness. A barium meal a month after admission failed to show any ulcer. There was no evidence of splenic anaemia or other blood dyscrasia at any time.

—I am, etc.,

Uxbridge, Middlesex. C. R. BAXTER.

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Treatment of Varicose Ulcer

SIR,—I was much interested in Dr. S. M. Rivlin's letter (Oct. 16, p. 723). I have been treating varicose ulcers since 1928, and my clinic numbers about fifty ulcer patients per week and some thirty or forty cases of varicose veins. I have improved and varied my own technique very considerably as the years have passed, and I have watched and noted with interest all other suggestions for the healing of ulcers, such as high ligation, multiple division or tributaries, excision of veins, and even lumbar sympathectomy.

One is driven back to the conclusion that ulcers of the legs are due fundamentally to the forces of gravity. The legs become congested either with old age (wearing out of the rubber elastic of the vein walls) or because of varicose veins. I feel most emphatically that the first essential in the treatment of a gravitational or varicose ulcer is tight compression and bandaging of the ulcers and tight bandaging of the lower leg. It is necessary of course to obliterate those veins with retrograde downward circulation which add to the congestion.

I myself get a very high percentage of cures by appropriately placed sites of injection of veins combined with the choice of an appropriate sclerosing fluid in each case, and above all by compression of the injected strip of vein after injection by elastic adhesive strapping applied over the vein.

My own technique in the cure of ulcers consists in putting zinc stearate or sulphanilamide powder into the ulcer base; then covering up the ulcer with "jelonet," applying calamine powder around the ulcer if there be any associated redness of the skin; then bandaging the whole leg from the toes to below the knee with "ichthopaste," placing external to this a pad of wool or sponge-rubber over the ulcer site, sometimes in a pyramidal manner, and then finally elastic adhesive strapping put on from above downwards to prevent rucking up by the stocking, combined with a back stirrup underneath this strapping.

Once the leg has been freed from its oedema it can be kept in this condition by the wearing of an elastic stocking or, better still, by an "elastolex" bandage, the latter being an improvement on "elastocrepe," for it has some strands of rubber fibre in it. As the months pass the leg resumes its normal proportions, owing to sclerosing of veins in certain cases, and the patient can sometimes abandon all support for the leg.

Recurrences of ulcers in fat old and middle-aged women are due to the lack of after-care in not keeping these legs supported. Admittedly I had about 5% of out-patient failures. I used to hospitalize these failures and give them open dressings. Certain cases even of these failed, but I succeeded in getting them ultimately healed by putting them to bed with the occlusive dressings above described. Finally, I must add that I have recently had some very gratifying results in the small percentage of resistant cases by putting them to bed and treating the ulcers with "viacutan" fluid.

One cannot emphasize too emphatically that destruction of given veins by any or all methods does not take away from the patient the tendency to have and develop other varicose veins; and it is only by appropriate tight and occlusive bandaging that ulcers can be healed and can remain healed.—I am, etc.,

Liverpool. STUART MCAUSLAND.

Pensions for Diabetics

SIR,—Those who like myself take an active interest in the pension struggles of the war disabled and of war widows cannot but be disturbed by the attitude expressed by Dr. R. D. Lawrence in his letter "Pensions for Diabetics" (Nov. 13, p. 875). It would seem to close the door finally on all claims involving diabetes.

Dr. Lawrence's book *The Diabetic Life* has long been the mainstay used to support these claims at tribunal hearings and High Court appeals therefrom. Now the supports have been cut away by the author himself. To this end he is recanting the phrase, "When shares go down in Wall Street diabetes goes up," and no doubt the interrelated sentences commencing, "There is also a large nervous element in diabetes," will be expunged as well. Is one to gather from Dr. Lawrence's letter that heredity and previous obesity are the only recognized causes of the disease, and that the numerous other factors mentioned in his book—infectious diseases, mumps, diseases of the liver, etc.—must now join nervous tension in the dustbin of discarded factors? As a matter of logic worry may be excluded as a cause because "otherwise the majority of humanity would become diabetic," but it would be equally logical to exclude previous obesity as a cause on the ground that otherwise the majority of the obese would become diabetic.

The cases of pension claimants show that diabetes and its complications may still produce disability through misfortune rather than lack of co-operation. Moreover, readers will recall the article by Drs. W. R. Gauld, A. L. Stalker, and A. Lyall (July 24, p. 194) dealing with the prevalence of renal complications in diabetes mellitus. How can one tell ex-Servicemen thus afflicted and war widows whose husbands died of the disease that diabetes is not a disability worthy of a pension, award, or support?

With commendable frankness Dr. Lawrence concludes the chapter on "Causation" in *The Diabetic Life* (1947 edition) thus: "To the majority of cases who ask why they developed diabetes I have to answer that I don't know." Let us hope that this of itself will be sufficient to give claimants the benefit of any reasonable doubt to which they are entitled under the royal warrant.—I am, etc.,

Boscombe, Hants. H. R. IVEL

Marxist Genetics

SIR,—Dr. C. D. Darlington's "review" (Nov. 13, p. 862) of Lysenko's pamphlet, *Soviet Biology*, seems to me to fall lamentably short of the standard of objectivity one expects in a scientific journal. The reviewer gives no hint of Lysenko's criticisms of contemporary biology. I remember learning (for my first M.B.) that evolution is due to mutations, and mutations "due to chance." When I began to read about physiological membranes I remember how odd the doctrine seemed that the germ plasm is independent of the soma, though they are only separated by membranes of greater or less permeability. If Lysenko's Marxism leads him, as it does, to doubt these inadequate doctrines, so much the better for Marxism.

Dr. Darlington does not even indicate that Lysenko's views tend to establish links between germ plasm, soma, and environment. He does not mention his experimental work. Although he strays from the exact subject of the book he is supposed to be reviewing, he does not indicate, what is emphasized for example by Professor Eric Ashby, that in Russia the peasants have so far lost their traditional conservatism (which still restricts development in our own dominions and colonies) that they welcome Lysenko's innovations with enthusiasm.

I do not presume to argue about biological theory myself, but I can see plainly that Dr. Darlington's review is not even intended to give readers a chance of knowing the issues. I can only conclude that it was written with a political purpose, that it was "pure propaganda," and therefore that it was much more suitable for the sensational newspapers than for the *British Medical Journal*.—I am, etc.,

London, S.E.24. H. M. ROSE.

SIR,—Dr. Ashley A. Robin's letter (Nov. 27, p. 955) on Marxist genetics makes strange reading. I certainly would be interested to see a report of the speeches of Lysenko's opponents at the Russian congress, and I would be even more interested to know if the opposition was "pre-arranged" or, if it were genuine, what happened to the opponents of Marxist genetics at the conclusion of the congress. I wonder if Dr. Robin has seen the letter from Sir Henry Dale in *The Times* of Nov. 26 announcing his resignation of the honorary membership of the U.S.S.R. Academy of Science and making special reference to Lysenko. According to Sir Henry, "Lysenko's own claims and statements make it clear that his dogma has been established and enforced by the Central Committee of the Communist Party as conforming to the political philosophy of Marx and Lenin." Dr. Robin styles himself not as a geneticist but as "one who can read." Might I respectfully suggest that he read some more.—I am, etc.,

London, W.4. JOHN C. C. LANGFORD.

Glamorous Labels

SIR,—The section of our profession concerned primarily with the conflict between man and his total environment rather than with the unfortunate results thereof seems determined to pour that good old wine, hygiene, from a multitude of new bottles bearing such eye-catching and glamorous labels as social medicine, human biology, human oecology or, in the utility and less stylish ranges, preventive medicine and public health.

Perhaps in this restless, inattentive age such thrusting pseudonyms are politically necessary; but hygiene, despite its prostitution to serve the parochial desires of V.D. prophylaxis or proprietary disinfectant vendors, remains for me the study of the avoidance of sickness and of the enhancement of health thus maintained—and this seems to cover the whole field without fuss or omission. Therefore I would like to see recorded in one place definitions of these subjects enunciated by those who profess them. In other words, what are their credentials?

At the same time I would appreciate an agreed table of definitions of the terms used by this fraternity. In reaching such definitions the mind must be purged of vague political phraseology and idealistic loose-thinking—in fact, cleansed of "a sort of stilted or pontifical woolliness in expression" which the experts say is a prominent feature in the thought disorder of schizophrenia.

In this respect the highest authority is itself an offender. In the *Report of the Ministry of Health for the year ended March 31, 1947* (p. 109), the principles of the World Health Organization are declared. The first two are: "Health is a state of *complete* physical, mental, and social well-being and not merely the absence of disease or infirmity," and, "The enjoyment of the *highest attainable standard* of health is one of the fundamental rights of every human being, etc." (my italics).

Three questions immediately present themselves. (1) What then is the absence of disease or infirmity? One cannot leave a terminological vacuum. (2) When, in fact, is disease or infirmity *really* absent except in a state of complete physical, mental, and social well-being? (3) If health is a complete state, how can one reach the highest attainable standard of it? Sir Ernest Gowers says in *Plain Words*, "It is a sign of slovenly thinking to qualify words that have an absolute meaning."

In short, the laudable fashion for plunging excitedly into the virgin jungle of health would be followed more satisfactorily by the man at the periphery if those already committed to this pastime appeared to know of each other's existence, to have correlated their plans of campaign, and to speak the same language when broadcasting their situation reports.—I am, etc.,

Morden Park, Surrey. DENIS H. D. BURBRIDGE.

Jelly-fish Stings

SIR,—The interesting letter from Dr. Frank R. Neubert (Nov. 6, p. 839) on the subject of jelly-fish stings recalls a paper on this subject published by Stuart and Slagle.[1] These authors point out that, "contrary to popular belief, the sting of a jelly-fish can be extremely dangerous, even fatal," and add that the effects are usually much more serious in tropical waters. They give the following description of the symptoms:

"Pain of a burning character at the site of contact, with redness followed by an urticaria-like weal about 10 minutes later; muscle spasms before the rash is well established, involving most of the trunk muscles and sometimes mainly in the extremities; a flushing of the skin; moderate dilatation of the pupils; congestion of the respiratory mucous membrane; a profuse, thin, mucous nasal and bronchial secretion; profuse lacrimation in severe cases; incessant cough with expectoration; spasm of respiratory muscles, leading to difficult respiration, and probably accounting for the patient's fear and anxiety which is frequently thought to be hysteria; and marked pain in abdomen and back, where large muscle groups are stony-hard with spasm."

Wade[2] reported the case of a patient who died from "suffocation" within a few minutes of being stung on the lower extremities, although he had never been submerged. There was visceral congestion and status lymphaticus.

As treatment Dr. Neubert used tincture of *Urtica urens* with apparent success, though it seems possible that the first sting may have conferred an immunity against subsequent ones. Old[3] gave morphine by injection and states that the native remedy was sugar internally and vinegar externally. Stuart and Slagle (loc. cit.) describe two patients who were stung by a "Portuguese man-of-war." In addition to an urticarial rash both men had severe muscular cramps, great difficulty in breathing, and oppression of the chest. Each was given an intravenous injection (10 ml.) of 10% calcium gluconate, with almost instantaneous relief of the dyspnoea and muscle cramps.

Apparently nothing is known about the nature of the toxic substances, although the above authors state that it is injected by means of tiny barbs which are contained in thousands of trigger hairs on the tentacles and which protrude on contact. The urticaria, the extremely rapid onset of generalized symptoms, and the equally rapid action of calcium injections certainly suggest an allergic reaction, but there is an opportunity for an interesting piece of research here analogous to the recent investigation of nettle stings.[4]—I am, etc.,

Basle, Switzerland. BRUNO PLOTKE.

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2 *Amer. J. trop. Med.*, 1928, **8**, 233.
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POINTS FROM LETTERS

Plain Words on Nursing Shortage

Mr. L. H. HORNSBY (Ministry of Labour and National Service) writes of Mr. W. S. Brindle's comments (Oct. 30, p. 800) one word: *Touché*.

Breast-feeding

Mrs. V. BENNETT (London, N.8) writes: I think Dr. Rachel Pinney (Nov. 13, p. 878) has made a very valuable point in suggesting that one of the major causes of lactation failure is outside interference in the tender emotional partnership of mother and newborn baby. I was a practising midwife for many years, and since my marriage and the birth of my own two children I have taken several private maternity cases. I did so on the understanding that the mothers under my care allowed the breast-feeding to be conducted after my own method, which is simplicity itself. Immediately after the birth and washing (the mother being fit enough) the baby is put to the breast, where usually it takes hold and gains comfort enough to sleep cosily in the crook of its mother's arm. A cot stands by the head of the bed so that, if the mother wishes, the sleeping baby can be put down within her reach. Both usually sleep for an hour or two. When the baby next wakens and cries it is again given to the mother with the instruction to give it the breast if it appears to be mouthing around for food. I find this feeding can be conducted in a semi-recumbent position, it being necessary for the nurse only to assist in making the pillows comfortable and supporting. This goes on day and night, with the baby regulating its own feed times and sleeping all the time between. Before three days the baby seems well satisfied with the colostrum it receives and even goes three or four hours without attention. I find there is very little breast engorgement on the third day, and I have never had a breast abscess from over-congested breasts or a failure to feed the whole nine months. The baby, needless to say, is relaxed and happy and never cries unless hungry or cold. . . .

Fumes and Colds

Dr. T. H. DURRANS (Bourton-on-the-Hill, Glos.) writes: I have read with interest the letter from Dr. G. C. Pether (Nov. 13, p. 879), and I think it may be of interest to him and other doctors to relate an experience covering over thirty years. In a chemical factory with which I was concerned we made among many other chemicals products from sulphur dioxide, and the air in the plant buildings where these sulphur dioxide products were made was always heavily charged with the gas. It was continuously found that the workmen in this plant were markedly free from the common cold and from "influenza." It therefore seems probable that the presence of sulphur dioxide in the saliva for periods of 8 hours or more daily has a protective effect. . . . It should be noted that other workmen working in parts of the factory remote from the sulphites plant did not enjoy the immunity.

Tendon Rupture and Rheumatoid Arthritis

Dr. PETER LONDON (London, S.W.15) writes: Dr. G. D. Kersley's report (Nov. 27, p. 942) of the spontaneous rupture of a deep flexor tendon in a patient suffering from rheumatoid arthritis prompts me to report a similar experience of my own in a woman of 66. In this case, however, rupture was traumatic, being due to the patient's jabbing petulantly at a push-button on her radio set, though such a stress seems inadequate as a cause of rupture of a normal flexor tendon. In her case the tendon was the deep flexor to the right middle finger; it was explored, as her left hand was almost useless and she was anxious to regain if possible fuller control of the digit. Rupture had occurred just proximal to the digital synovial sheath, and as there was no sign of fraying of the tendon it must be assumed that rupture was due to some other sort of weakness. Simple suture was carried out, but the amount of movement regained was very small.

Obituary

J. H. SEQUEIRA, M.D., F.R.C.P., F.R.C.S.

Dr. James H. Sequeira, who was for many years consulting physician to the Skin Department of the London Hospital, died in Kenya at the age of 83. He had a world-wide reputation as an authority on diseases of the skin.

James Harry Sequeira was born in London on Oct. 2, 1865, and educated at King's College School. Entering the London Hospital with a science scholarship in 1884, he qualified in 1889, graduated M.B. in 1890, and proceeded M.D. a year later. He was a dresser to Mr. Frederick Treves, as he was then, and he was also much influenced by Sir Stephen Mackenzie, whose house-physician he became. He took the F.R.C.S. in 1893, the year in which he won the Hutchinson Prize, and he was elected F.R.C.P. in 1905. Dr. Sequeira studied at Vienna some years after qualifying, and subsequently he worked under Niels Finsen in Copenhagen. He was responsible for translating Finsen's book on phototherapy in 1901, and at the London Hospital, where he was appointed assistant physician in 1902, he set up a light therapy department which was the first of its kind in this country. He also wrote at this time some of the early reports on the treatment of epitheliomata by *x* rays and radium. In 1905 Dr. Sequeira published *An Elementary Treatise on the Light Treatment for Nurses*. His well-known textbook *Diseases of the Skin* appeared in 1911 and reached a fifth edition in 1947. Dr. Sequeira was for many years editor of the *British Journal of Dermatology and Syphilis*, and he contributed many papers to the medical press.

When he retired from the active staff of the London Hospital in 1927 Dr. Sequeira went out to Kenya but continued to take an interest in medical work of all kinds and particularly in leprosy. He was president of the Kenya Branch of the British Medical Association in 1930–1 and again in 1933–4. He was also editor for over ten years of the *East African Medical Journal*. When war broke out in 1939 his services were again in demand. In the 1914–18 war he had acted as consultant in dermatology to the military hospitals in London. During the recent war he served in the same capacity hospitals in East Africa. Dr. Sequeira was one of the most active members of the late Lord Trevethin's Committee on Venereal Disease, and was at one time chairman of the executive committee of the Society for the Prevention of Venereal Disease. He was also president of the Section of Dermatology of the Royal Society of Medicine in 1925–7, and a corresponding member of the French and Danish dermatological societies.

Dr. W. J. O'Donovan writes: Between the two wars a frequent sight in the London Hospital was the short, very sturdy, white-haired figure of Dr. Sequeira walking gravely from bed to bed or across the gardens to the out-patients. Throughout his professional career Dr. Sequeira was distinguished by the qualities of gravity and leadership, and his clinical acumen was outstanding. From Johannesburg to Toronto, in Leeds, Charing Cross, the Royal Free, and in the London Hospitals his teaching is a tradition carried on by his own professional sons. Before taking up dermatology—and he was the first dermatologist appointed as such to the London Hospital—he was fully trained in both medicine and surgery and was almost unique in holding later the fellowship of both the ancient Colleges. His textbook was an early classic of modern dermatology and when it appeared was unusually lavish in well-chosen illustrations.

Dr. Sequeira was a master of the treatment of lupus and a pioneer in this country in the clearance of the school population from tinea capitis by an organized mass *x*-ray attack upon infected heads in East London. These were the cases ascertained and sent for treatment by the London School Medical Service in its earliest days. He was a pioneer in light therapy, in *x*-ray therapy, and in the use of radium for skin diseases, and dermatologists trained by him in this technique have maintained his special interest and competence in radiotherapy. Dr. Sequeira served his generation as secretary of the learned societies and presided with great urbanity and decorum when presidential chairs fell to his lot. He maintained the friendliest of relations with French and Danish colleagues and was frequently visited at his clinic by American dermatologists. His patience in teaching generation after generation of undergraduates was his outstanding virtue. His regularity in hospital attendance was a model of conscientious attention to his voluntary duties. So valued was his teaching that it was common for budding specialists to attend his out-patients clinic twice a week for two years to gain his cachet and to absorb some of his experience and diagnostic methods. His judgment of others was always kindly, and he was ceaseless in encouraging the youngest of his juniors to make original observations and to try whilst they had the opportunities of hospital life to add to knowledge.

At a time when the London Hospital staff included men of outstanding metropolitan distinction Dr. Sequeira fully held his own, and his memory is reverenced by hundreds of practitioners and in countless of homes, for his benignly judicial and kind personality made a lasting impression on all who met him. Coronary disease attacked him in his eighties, and to his wife and his two adopted children we offer our deepest sympathy.

Dr. John T. Ingram writes: The portly figure and gentle, courtly manners of Dr. Sequeira reflected his quiet pride in his ancestry. He was the sixth, in direct descent, of a line of doctors, and he wore on his little finger the "morning ring" of one of his doctor ancestors born in the year of the Great Fire of London. When Napoleon invaded Portugal a great-grandfather of Sequeira came to London in the train of the Prince Regent of Portugal and was physician to the Portuguese Embassy to the Court of St. James's. Sequeira was born and educated in London and was immensely proud of his association with the London Hospital. He had wished to be a physician, being particularly interested in cardiology, but circumstances fortunately determined his being asked to establish a department of dermatology. In his training he had attended lectures by Sir Jonathan Hutchinson and had clerked for Hughlings Jackson. He had little money, but he achieved a remarkable postgraduate education. He held resident appointments under Stephen Mackenzie, Warren Tay, and Herman, and was for four years demonstrator in anatomy under Arthur Keith and Wood Jones. He followed this with two years as medical registrar and two years as medical tutor, an apprenticeship of eight years' teaching appointments. He was proud of his associations with Leonard Hill and Lindemann (later Lord Cherwell), and recalled with pleasure tea-parties with William Bulloch and Paul Fildes in the bacteriological department.

Two great milestones in medical history influenced Sequeira's work—the physiotherapeutic advances of Finsen and the researches of Ehrlich. He spoke with affection of the interest and encouragement of Sidney Holland (Lord Knutsford) at the London Hospital, and he soon attracted disciples from all over the world and especially from the Dominions and Colonies. He was meticulous in his attention to hospital duties, and kind and generous and helpful to all who worked with him. He would have liked a full-time post at the London Hospital, for he disliked the monetary side of medical practice, but the offer came too late. He was, however, strongly opposed to a whole-time medical service for the nation. Sequeira greatly admired Radcliffe Crocker's textbook, but his own work was the first to leave the morphological approach to skin diseases and attempt an aetiological classification. He was fond of music, and though he remained a busy man to the end, alert and interested in every new dermatological work, he greatly appreciated the opportunities for indulging his interest in music which came with retirement. He said that he owed everything to two women—his mother and his wife. The devoted affection of his wife undoubtedly enabled him to contribute from his wisdom to the work he loved into a ripe old age.

E. LEWIS LILLEY, M.B., F.R.C.S.

Dr. Ernest Lewis Lilley, who was 72, died quite suddenly in his consulting room on Nov. 22 from coronary occlusion. He was a member of an old Leicester family and was educated at the Wyggeston School, Leicester. He obtained an entrance scholarship at Charing Cross Hospital and qualified in 1899, graduating M.B., B.S. in 1901 and taking the F.R.C.S. two

years later. He was successively house-surgeon, house-physician, and R.M.O. at Charing Cross Hospital.

In 1904 Dr. Lilley came to Leicester, taking over the practice of Dr. C. Nuttall. In his early years he took a great interest in *x*-ray work, and this stood him in good stead during the first world war. He was in charge of the Leicester and Leicestershire Maternity Hospital at its opening in 1904, and he remained in control till it was taken over by the Leicester Royal Infirmary in 1940. In addition to the ordinary routine work of the hospital, including many difficult cases, he trained and lectured to succeeding generations of maternity nurses and midwives. Dr. Lilley was a member of the board of management of the Leicester Public Medical Service, later becoming chairman, and finally president in 1938, which post he held until his sudden death. He was a member and later vice-chairman of the Local Medical and Panel Committee from 1911. He was also a member of the Local Insurance Committee under the N.H.I. He joined the Leicester Medical Society when he started practice, and was elected president in 1928–9.

During the first world war Dr. Lilley was surgeon to the Fifth Northern General Hospital, Leicester, and later went to Egypt, where he was radiologist to the Citadel Military Hospital, Cairo. At the end of the war he returned to Leicester and continued his work until his retirement from general practice in 1939. He was then appointed chairman of the Leicester Recruiting Medical Board. He also continued to act as anaesthetist to the Leicester School Clinic and actually gave several anaesthetics on the morning of his death. Dr. Lilley was an examining factory surgeon and medical referee under the Workmen's Compensation Act and National Insurance Act. He was always a keen supporter of the British Medical Association, and was a member of the Council from 1931–43 and of the Insurance Acts Committee from 1921–46. He was chairman of the Leicester and Rutland Division in 1927–8, and he was a member of the Journal Committee from 1921–32. He also served on the Therapeutic Substances and National War Formulary Commission of the Ministry of Health, and became its chairman. He was a member of the council of the Medical Defence Union.

Dr. Lilley, as a member of the council of Leicester University College, was largely responsible for the foundation of the music department there, especially the music library, to which he constantly added fresh books. He was on the council of the Leicester Literary and Philosophical Society and became president in 1932. Only a fortnight before his death he read a paper on "Inductive Reasoning" to the philosophical section. Apart from medicine his greatest interest was music. He was president of the Leicester Chamber of Music and a member of the Philharmonic Society. He had been choirmaster and organist at the Great Meeting Unitarian Chapel, Bond Street, Leicester, for about forty years. Dr. Lilley was an outstanding personality with unbounded energy. He was always ready and anxious to do his best for anyone in difficulties. He was generous both with his time and money, and went out of his way to help others. His advice was often invaluable and always based on a considered and sound judgment. —E. W. H.

Dr. C. L. Somerville writes: With the death of E. Lewis Lilley the medical profession in Leicester has lost the most outstanding personality among the older generation of doctors. Endowed with an iron constitution and tremendous energy, his capacity for work was a source of amazement to lesser mortals. Unfailingly cheerful, his chuckling laugh punctuated his conversation. His mental calibre matched his energy and together with an acutely retentive memory made him master of a great diversity of subjects from pure science to higher mathematics. Fifty years after his days as a demonstrator of anatomy he still had a clear grasp of abstruse details which few practising surgeons of to-day could approach, let alone equal. As was to be expected from a man of such attainments, his pursuits and hobbies were intellectual, and of these music held first place. Outdoor sport had no attractions for him, and I doubt if he ever went for a country walk. The live theatre and cinema saw him but seldom, but he rarely missed the concert hall or chamber music recital or the Three Choirs' Festival, and he knew the organ lofts of churches and cathedrals up and down this country and abroad.

In medical matters Dr. Lilley's opinion was sound, but in later years he tended to be rather conservative. His wide medical knowledge and vast experience were everywhere recognized, and his simple and likable traits endeared him to an immense number of patients and friends. He was probably at his heyday about the time of the B.M.A. Annual Meeting in Australia in 1935, and many colleagues will remember him on the tour across Canada and the U.S.A. Though he retired from general practice in September, 1939, he kept on several appointments, and throughout the war years he undertook long days of exacting work as chairman of recruiting boards.

F. H. S. CURD, Ph.D., B.Sc.

Francis Henry Swinden Curd, who died on Dec. 2 in Stockport Infirmary at the early age of 39 as a result of a railway accident, was not a member of the medical profession but a chemist on the research staff of Imperial Chemical Industries. His death is a serious loss to chemical research and to chemotherapy in this country, for since 1933 he had been engaged on the production of new chemicals, and during the war he was the leader of the team which synthesized the antimalarial drug proguanil or, as it was formerly called, paludrine. This compound is the least toxic of the known antimalarials, and, though its potentialities are not as great as was at first hoped, its chemical structure represents an entirely new departure in drugs with an action in malaria. Its synthesis was developed by logical steps from mepacrine, the pyrimidine nucleus being first substituted for the acridine ring; later the pyrimidine structure was replaced by a guanidine, leading finally to the formation of N_1-*p*-chlorophenyl-N_5-*iso*propyl-biguanidine. These investigations Curd and his colleagues reported at length in a series of important communications to the *Journal of the Chemical Society* and in the *Annals of Tropical Medicine and Parasitology*. In 1947, with D. G. Davey and F. L. Rose, he was awarded the Gold Medal for Therapeutics of the Worshipful Society of Apothecaries. Before joining the staff of I.C.I., Curd worked for a time in the laboratories of the School of Hygiene and Tropical Medicine, and it was here that his interest was originally aroused in the chemotherapeutic control of tropical diseases.

Dr. John Kerr writes: There was no greater personality in the County Palatine of Chester than Dr. Lionel James Picton, of Holmes Chapel. Physically a man of rotund build, he had the stoop of the scholar, a kindly countenance with eyes which looked straight at you, and a mental and physical alertness which belied his years. The statement in your excellent obituary (Nov. 27, p. 960), "though he never published a book," is incorrect, for his book *Thoughts on Feeding* was published by Faber and Faber in 1946. As secretary of the Local Medical and Panel Committee he instituted an investigation by the committee into maternal morbidity in the county of Cheshire. Consequent upon this investigation and the written evidence of Sir Robert McCarrison relative to the important part nutrition played in maternal fitness, the Local Medical and Panel Committee decided to proclaim to the people of Cheshire that the main factor in maintaining health was sound nutrition. Dr. Picton's natural genius produced the "Medical Testament" in which he reviewed their experience of twenty-eight years of medical benefit under the National Health Insurance Act. He proved that the Act had failed in one of its main objects—the prevention of sickness. Dr. Picton was an agriculturist of repute and contributed much valuable work on the rearing of livestock. Picton was an advocate of raw milk, and maintained that the great nutritional need of the community was an ample supply of clean, fresh raw milk, which could be obtained by the hygienic handling of milk from the healthy cow to the consumer. Picton was also deeply interested in soil fertility. He contended that, in so far as human health is dependent upon the quality of the food which the body requires, so is the food, whether animal or vegetable, dependent on the soil which sustains it. He has shown that the method of composting and returning the whole of the animal and vegetable refuse produced in the activities of a community to the soil results in the health and productivity of crops and of the animals and men who feed thereon. To this end he organized, on behalf of the Panel Committee, a county garden competition for cottage gardens and allotments to inculcate the much greater use of vegetables in the food of the people. Dr. Picton's gift of lucid and interesting exposition as a writer enabled him to undertake on behalf

of the Panel Committee the editorship of the *Compost News Letter*. This quarterly was the outcome of much correspondence from all over the world consequent upon the publication of the "Medical Testament." It is by men such as Lionel J. Picton, with their scholarship and broad culture, that village life in England is made so delightful. The village of Holmes Chapel, in Cheshire, with its fourteenth-century church, its inn, and its ancient traditions, has indeed been fortunate. Dr. Picton leaves a widow who all through her married life devoted herself to his care. She bore him three sons and three daughters, and two of the sons are now following the profession of their father, one of them carrying on the practice in Holmes Chapel.

Dr. SAMUEL ROBERT HUNTER, who died on July 9, was born in Belfast on March 3, 1877, and was educated at the Royal Belfast Academical Institution and Queen's College, Belfast. He took his B.A. degree in the Royal University of Ireland in 1899 with honours in chemistry and physiology, graduated M.B., B.Ch. in 1902, and proceeded M.D. in 1905. He was resident house-surgeon and extern surgeon in the Royal Victoria Hospital, Belfast, before settling down in private practice at Dunmurry. Here, by his genial personality and charming manner, Dr. Hunter quickly built up a large practice which extended far beyond the boundaries of his immediate district. He took a great interest in local medical affairs, was a life-long member of the B.M.A., and a fellow and president of the Ulster Medical Society. He volunteered for service with the R.A.M.C. in the first world war, and served most of the time in Salonika and the Middle East. On demobilization Dr. Hunter returned to Dunmurry and espoused the cause of the ex-Serviceman. He was president of the Dunmurry Branch of the British Legion from its inception until his death. His leisure was mainly devoted to golf, and he was a past captain of the Dunmurry Club. Dr. Hunter's health finally broke down under the stress of work, and in 1945 he retired from active practice and spent his days overlooking his beloved golf-links. He leaves a widow, two sons (Dr. G. A. C. Hunter and Lt.-Comdr. Hunter, R.N.), and one daughter.—J. G. J.

Dr. LOUISA HAMILTON, who died on Nov. 24, went to the London School of Medicine for Women in 1893, and during her first year began the course for the L.S.A., as the Royal Colleges were not open to women. In 1900 she obtained the M.B., B.S. degree of London University with honours in medicine and obstetrics, and in 1906 she proceeded M.D. For a few months after qualification she attended the out-patient and in-patient clinics at Great Ormond Street Hospital for Sick Children. She became a house-surgeon at the Elizabeth Garrett Anderson Hospital in 1901, house-physician there in 1902, and house-physician at the Royal Free Hospital a year later. In 1903 she was appointed demonstrator in anatomy at the London School of Medicine for Women. She started private work in 1905, at first in general practice. She worked for seven years in Brunswick Place, and in 1912 moved to Nottingham Place, where she was well known for twenty-one years as a physician. She held the post of part-time pathologist at the Elizabeth Garrett Anderson Hospital, and later was appointed a member of the staff of that hospital, first as assistant physician, then physician, and finally as senior physician. This post she held till 1936, when she retired. In addition, for many years Dr. Hamilton was medical officer to the North London Collegiate School for Girls, the C.E.Z.M.S., and the Methodist Missionary Society. When she retired she went for a trip to Jamaica in 1937, and on the return journey contracted the illness which ultimately proved fatal. Dr. Hamilton had many friends and interests. She had the Scottish tenacity of purpose that is satisfied only with the best. This was shown in her medical work but also in the gradual development of her lovely garden in Buckinghamshire. She was an excellent hostess, and excelled at cooking. Many generations of students and house-physicians will remember her generous hospitality. Writing as colleague, friend, and patient, I can speak from personal knowledge of Dr. Hamilton's loyal and sane help. She took a wide view of her patients' needs, and infused into them some of her own courage and common sense. She knew that a great deal goes to the remedy of the ills that we meet, and by her wisdom and sanity she helped many people in many different places, and they all have cause to remember her with gratitude. Louisa Hamilton played a losing game for years with heroic courage. Her loyalty, helpful common sense, and generosity will be remembered.—E. B.

A memorial service for the late Dr. Louisa Hamilton will be held at St. Pancras Church, Upper Woburn Place, London, W.C., to-day (Saturday, Dec. 11) at 11.30 a.m.

Medico-Legal

TOO SHORT A GESTATION PERIOD

The period of 349 days was recently accepted as a possible gestation period by the Court of Appeal.[1] Subsequently Mr. Justice Ormerod, in a case heard in the Divorce Court on Nov. 17, accepted expert medical evidence that it was impossible for a normal child to be born after 340 days.[2] On Nov. 26 Mr. Justice Vaisey had to consider what appeared to be a short period of gestation. This was a case under the Guardianship of Infants Acts, 1886 and 1926, in which he allowed an appeal from an order of a Metropolitan magistrate making an order for payment by a husband of maintenance for a child. Mr. Justice Vaisey allowed the appeal[3] on the ground that on the evidence from an Army records office, and from hospital case-sheets, the husband against whom the maintenance order was made could not have been the father of the child. He returned from two years' service overseas on Jan. 29, 1945, and had intercourse with his wife on Jan. 31. The wife was delivered of a child on Aug. 8, 1945, an alleged period of gestation of 188 days. Evidence was given that the child was perfectly normal. His Lordship was therefore driven to the conclusion that the child could not have been the offspring of the husband, and the order for maintenance was therefore discharged.

BERYLLIUM AS A CAUSE OF DEATH

What is said to have been the first fatal case of beryllium poisoning in Great Britain was recently the subject of an inquiry by the East London coroner, Mr. W. R. Heddy.[4] A physicist aged 36, employed by a firm at Edmonton, had been working with beryllium oxide from December, 1941, to December, 1942. He was engaged in work on the development of fluorescent lighting. He remained apparently well until 1945. He then complained of a cough and loss of weight and was eventually admitted to the London Hospital, where he died on Nov. 4. Necropsy showed that death was due to beryllium poisoning.

Beryllium, which was discovered in 1797, was very little known before 1916 and has been of prime economic importance only since 1940. The toxic hazards of beryllium were discussed in an annotation in this *Journal*,[5] and subsequently in a leading article[6] an account was given of cases of beryllium poisoning reported from America. At that time among 170 cases of poisoning the chief manifestations were dermatitis, chronic skin ulcer, and inflammatory changes in the respiratory tract, producing in extreme cases a diffuse pneumonitis. A chemical pneumonitis developed in 38 of these workers, of whom 5 died.

[1] *British Medical Journal*, Nov. 6, p. 840.
[2] Ibid., Nov. 27, p. 962.
[3] *The Times*, Nov. 27, 1948.
[4] Ibid., Dec. 6.
[5] *British Medical Journal*, 1943, **2**, 460.
[6] Ibid., 1946, **2**, 231.

Medical Notes in Parliament

National Service

The National Service (Amendment) Bill, which was read a first time without debate in the House of Commons on Nov. 24, proposes to increase the period of whole-time service of men called up under the National Service Act, 1948, from twelve months to eighteen months, but to reduce their total period of whole-time and subsequent part-time service in an auxiliary force from seven years to five and a half years. It is further proposed that registered medical practitioners and persons registered in the *Dentists' Register* under the Dentists' Acts, 1878-1923, shall be liable to be called up under the National Service Act up to the age of 30 instead of only up to the age of 26, which applies generally.

Inadequate Remuneration

Mr. BEVAN told Sir ERNEST GRAHAM-LITTLE on Dec. 1 that he was not aware of severe hardships suffered by doctors as a

consequence of inadequate remuneration under the National Health Service. He added that this remuneration was based on the recommendations of the Spens Committee and had been agreed upon with the profession. The initial distribution of the total amount of money made available was giving rise to temporary difficulties. These he was discussing with representatives of the profession.

Sir ERNEST GRAHAM-LITTLE also asked Mr. Bevan if he knew that his directive to executive councils to the effect that it was not his intention that payments from the Inducement Fund should be made in cases where difficulty could be met by a fixed annual payment would, in fact, result in a general lowering of the capitation grant; and whether he would withdraw this directive and allow such payments to be met from the Inducement Fund.

Mr. BEVAN replied that he saw no reason to alter these arrangements.

Amending Bill

Mr. BEVAN, replying on Dec. 2 to Sir HENRY MORRIS-JONES, said the matter of an amending Bill to the National Health Service Act had been under discussion with representatives of the medical profession. When full agreement had been reached—or when full agreement had not been reached—a Bill would be presented to the House. Sir Henry asked whether the amending Bill would deal with anomalies in the Act which had been clearly demonstrated. Mr. BEVAN said Sir Henry had better await the Bill.

Mr. SOMERVILLE HASTINGS asked if Mr. Bevan knew of the many expressions of satisfaction received from all sections of the community.

Mr. BEVAN said that undoubtedly many millions of people had already benefited under the Act. He hoped that when the Report of the Ministry of Health came to be presented to Parliament it would give an objective review of what had happened.

Sir HENRY MORRIS-JONES gave notice that he would raise this matter on an adjournment of the House.

The Doctor's Bag.—Sir WALDRON SMITHERS on Nov. 30 asked the Chancellor of the Exchequer, in view of the extra pressure of work placed on doctors under the new Health Act, to exempt from purchase tax articles necessary for the use of doctors in their professional duties, especially the doctor's bag. Sir STAFFORD CRIPPS refused to do this. He said it was not possible to give doctors special privileges for the few chargeable articles they used professionally.

Certificates for Spectacles.—Dr. SANTO JEGER on Dec. 2 asked the Minister of Health whether, in view of the pressure of work on doctors, the long waiting in doctor's waiting-rooms, and the formal nature of the certificates involved, he would remove the necessity for patients requiring to have their eyes tested by opticians to obtain doctors' certificates saying so. Mr. BEVAN replied that this requirement was instituted in the light of advice received from the medical profession. He would not feel justified in abolishing it except on professional advice.

The Services

Surgeon Lieutenant-Commanders R. E. King, W. I. D. Scott, and R. T. Gaunt, R.N.V.R., have been awarded the R.N.V.R. Decoration.

The President of the U.S.A. has conferred the Bronze Star Medal upon Lieutenant-Colonel (Temporary) E. Samuel, Major (Temporary) A. Noble, M.C., and Captain (Temporary) R. W. Preston, R.A.M.C., in recognition of distinguished services in the cause of the Allies.

The King of the Hellenes has conferred the following decorations in recognition of distinguished services in the cause of the Allies:

Grand Cross of the Royal Order of the Phoenix.—Major-General J. C. A. Dowse, C.B., C.B.E., M.C., late R.A.M.C.

Commander of the Royal Order of the Phoenix.—Captain A. M. Boyd, R.A.M.C.

The Prince Regent of Belgium has conferred the following decorations in recognition of distinguished services in the cause of the Allies:

Officer of the Order of Leopold.—Colonel (Temporary) J. P. J. Jenkins, O.B.E., T.D., R.A.M.C.

Croix Militaire 1st Class.—Major F. H. Newland, Major (Temporary), E. James, and Captain S. Howe, R.A.M.C.

Croix Militaire 2nd Class.—Major (Temporary) W. Barnes, R.A.M.C.

DEATHS IN THE SERVICES

Sir Matthew Fell, K.C.B., C.M.G., writes: My old friend, Lieut-Col. J. C. JAMESON, R.A.M.C., died last July after a long illness patiently and philosophically borne. He was the eldest son of the late Surgeon-General J. Jameson, C.B., K.H.S., who was Director-General of the Army Medical Service at the outbreak of the South African war, and was a graduate of Edinburgh University. I met him first at the Orange River Bridge in November, 1899, when Lord Methuen's Force was concentrating for the advance on Kimberley; and after that he continued under the same commander until 1902, wandering throughout the West of the Orange Free State and Western Transvaal. Jameson had previously served in the Afridi Campaign on the North-west frontier of India, and was later to serve with me throughout the first world war. But it was the close daily contact of three years on the veldt that formed our friendship, which lasted without a break to the time of his death. He was a keen golfer and also a fisherman, and after his retirement we had many happy days together. He never married, but children and young people loved him. Hating the limelight, self-effacing, careless of his appearance, almost hyper-conscientious in his professional work, anxious to give of his best at work or play, he was a truly lovable character, and the world is the poorer for his passing.

Universities and Colleges

UNIVERSITY OF CAMBRIDGE

In a Congregation held on Nov. 27 the degree of M.A. was conferred on James Wilson Millen, M.D., University Demonstrator in Anatomy. The degree of M.D. was conferred on T. St. M. Norris (by proxy) and D. S. Short.

UNIVERSITY OF DURHAM

Sir Henry Dale, O.M., F.R.S., will give the fourth Rutherford Morison Lecture in the Royal Victoria Infirmary, Newcastle-upon-Tyne, on Thursday, Jan. 20, at 5 p.m. His subject is "Physiology and Surgery."

UNIVERSITY OF LONDON

The following candidates have been approved at the examination indicated:

POSTGRADUATE DIPLOMA IN PSYCHOLOGICAL MEDICINE.—*With Mental Diseases (Psychiatry) in Part B:* I. R. C. Batchelor, D. D. Howell, D. W. Liddell, D. L. Murti Rao, A. J. P. Oldham, J. W. T. Redfearn, Ethel E. Robertson, J. T. Robinson, D. Stafford-Clark, A. C. Tait, R. W. Tibbetts. *Part A:* El T. Elmahi, E. S. Goller, Joan I. Hallinan, J. M. Macdonald, J. Merry, H. R. Morton, P. Pinkerton, I. M. Shepherd, J. Todd, L. P. Varma.

THIRD M.B., B.S.—[14]Elizabeth Bennett, [14]P. Chadwick, [13]K. M. Citron, [15]B. Creamer, [15]A. A. Eley, [15]H. J. A. Hahn, [13]Cherry D. Heath, [13]Joan E. Jermyn, [13]G. D. Starte, M. S. M. Adams, Maureen B. Adams, C. P. T. Alexander, A. M. Angel, Marion M. Ashforth, R. N. H. Askham, D. S. G. M. Bailey, J. R. Ballantyne, T. W. Barnes, Barbara Baxter, S. J. Beales, M. D. Begley, S. Benaim, G. C. Blake, Hazel C. Blomfield, W. R. Bodenham, Edda L. I Boesen, J. M. N. Boss, J. H. Boydell, Margaret L. M. Bridges Ethel A. V. Brooks, P. D. Bryant, R. Buri, F. P. Cassidi, I. Chance, J. A. Cheese, D. W. Clark P. S. Clarke, I. H. Colley, A. A. Collis, A. J. P. Crowden, Mary E. Curling, H. W. D. Davies, J. H. Davies, T. D. L. Davies, L. R. Davis E. El Dawe, D. C. Deuchar, Daphne M. Dowlen, E. M. Edwards, Evelyn S. Elliott, Hilary J. Elphick, D. M. Evans, E. Evans, D. C. Faull, K. J. Fisher, D. G. Fleck, C. A. Foster, P. B. Foxwell, K. Froome, G. G. Garlick, Phyllis A. George, A. M. Goldthorpe, K. C. D. Gordon, D. B. Goss, R. L. Gothilf, E. W. Graham, A. H. Griffith, M. W. J. Grummitt, D. B. Gunasekara, June M. S. Harrington, D. F. N. Harrison, R. D. C. Hart, G. E. Haward, P. W Head, J. L. Herbert, D. A. Hodgson, E. R. Hodgson Todd, H. D. A. Hope, Pamela C. B. Hopkins, D. A. Howell, F. H. D. Hutter, A. H. Jack, D. W. James, Barbara J. Jeffrey, F. H. W. Johnson, C. R. Jolly, D. H. Jones, E. F Jones, J. S. Jones, C. Joseph, D. H. Judson, G. Kaufman, R. A. Keable Elliott, Zeē T. Kelly, H. R. Ker, M. R. R. Khan, F. R. S. Knight, P Lancer, B. H. Lawrence, J. C. S. Leverton, D. C. Lindley, R. H. Longton, G. N. Lumb, B. Lytton, W. E. Macbean, R. P. C. MacDonald, T. McKendrick, D. Mendel, René L. Mendez, Leela Menon, Marie D. Merchant, D. K. Morgan, Elizabeth M. Mostyn, J. G. Neville, Margaret C. Newmark, P. B. O'Neill, M. W. Partington, Jacqueline I. C. Payne, G. W. Piper, D. G. Price, E. R. Price, K. J. P. Price, V. G. Radclyffe, G. S. Ratnavale, I. Redstone, E. G. Rees, W. J. St. E.-G. Rhys, B. W. Richards, H. R. C. Riches, Janet P. Rickard, P. P. Rickham, D. Rossdale, D. P. Rough, D. G. Rushton, M. V. Salmon, A. C. E. Sandiland, B. Schwartz, M. L. J. Segall, J. C. Sherris, B. P. Skinner, J. F. Skone, G. B. Smith, D. B. Spanton, Diana H. Spears, Rosemary Stephens, S. Sternberg, M. T. Sweetnam, Hilda J. Tanner, D. G. Taylor, T. Taylor, Anita J. Thomas, O. G. Thomas, J. V. Thurston, P. H. Tribe, A. A. Turner, R. J. Vale, J. Vance, P. R. Wagner, Daphne M. L. Walters, Mary B. Watson, F. E. Weale, Joan C. Wells, Margaret M. Whitaker, H. Williams, W. J. Williams, M. B. Wingate, Mary I. Wray, J. Zamler.

[1] With honours. [2] Distinction in hygiene and forensic medicine. [3] Distinction in medicine. [4] Distinction in applied pharmacology and therapeutics. [5] Distinction in surgery.

Dr. E. R. Boland has been elected Dean of the Faculty of Medicine for the period 1948–50.

The title of Reader in Experimental Pathology in the University has been conferred on Peter Alfred Isaac Gorer, D.Sc., M.R.C.S., L.R.C.P., in respect of the post held by him at Guy's Hospital Medical School.

UNIVERSITY OF WALES

The following candidates for the degrees of M.B., B.Ch. at the Welsh National School of Medicine have been approved at the examination indicated:

MEDICINE.—Sarah A. Chard, N. V. Chivers, D. P. Davies, G. J. Davies, E. H. Evans, E. J. Hargadon, J. M. E. Hyde, T. D. Jones, Lilian M. Morgan, G. M. Reynolds, J. M. Richards, Esme S. Rogers, Mary C. Sumption, G. Thomas, J. A. Wilkinson.

PHARMACOLOGY.—Joyce M. Bennett (with distinction), L. V. Chubb, S. I. Davies, Nansi G. Gwynne, C. W. J. Hunt, D. T. Jones, Rachel B. J. Lewis, Mary I. Lloyd, J. E. Merrell, Janet M. Moffat, Elizabeth M. M. Price, T. B. N. Richards, A. P. Thomas, D. S. Wood.

ROYAL COLLEGE OF PHYSICIANS OF EDINBURGH

At a meeting of the College held on Dec. 2 Dr. W. D. D. Small was elected President and Dr. W. A. Alexander was nominated Vice-President.

ROYAL COLLEGE OF PHYSICIANS OF IRELAND

The following were admitted to the Membership of the College on Nov. 5: P. B. B. Gatenby, M. Ghosh, R. J. Kernohan, R. M. Peet, R. W. Temple.

ROYAL COLLEGE OF SURGEONS IN IRELAND

The following have received the Fellowship of the College: D. V. Kneafsey, J. J. O'Shaughnessy, C. I. Wilkinson, W. H. de W. De Wytt.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

At a meeting of the Council of the College held at College House on Nov. 27, with the President, Sir William Gilliatt, in the chair, the following were formally admitted to the Membership of the College: T. M. Abbas, Agnes U. Campbell, Margaret Fitzherbert, R. A. Irani, Mary S. Jolly, P. M. Naidu, C. G. Nairn, M. S. Qureshi, Helen M. Russell, S. A. Siddiki, P. de S. Wijesekera.

The William Meredith Fletcher Shaw Memorial Lectureship for 1949 was awarded to Professor R. W. Johnstone, of Edinburgh. Leverhulme Scholarships tenable for one year were awarded to F. Reid, for research into *x*-ray diagnosis of placenta praevia, the relation between foetal position and the placental site, and an attempt to develop a new method of amniography, and to C. J. Mackinlay, for research into the investigation of chronic infections of the vulva.

The following were granted the Diploma in Obstetrics of the College:

T. R. Aggarwal, Patricia M. Aikman, Emma M. H. Albinson, N. Alders, Beryl G. Anscombe, D. J. Atherton, R. K. Banerjee, A. S. Barling, J. W. Bartrum, K. S. P. Blatchley, V. Y. Bockner, Mary M. M. Boyd, Mollie A. Brown, Joan M. Burrell, M. Byrne, G. S. Caithness, Elspeth S. K. Campbell, Harriett A. Cawthorpe, Dorothy B. Charlton, G. R. Clare, M. H. Clark, Nancy G. Clegg, Shirley Clifton-Smith, G. R. Connolly, Margaret M. Coughlan, Vivienne A. Croxford, P. N. Cunliffe, R. G. Dewhurst, J. J. B. Dias, Mary Douglas, Aileen P. M. Dring, E. W. Duncan, Violet M. East, W. M. Edwards, Louise E. Elbert, Mary R. Ellis, W. I. Emslie, C. J. Farr, T. R. Farrimond, Mary E. G. Feetham, G. S. Foster, Frances M. Fountain, Maud M. Frankland, T. P. S. Frew, S. Galande, H.-J. B. Galbraith, P. D. Gange, H. L. Gardner, Joy M. Gardner, W. F. T. George, M. Gold, D. S. M. Graham, F. G. Grant, Jean A. Grant, Violet H. Gray, C. R. H. Green, A. G. Grossett, M. J. L. Hassall, J. K. Hawkey, Josephine M. R. Heber, F. W. Henderson, J. Hendry, Mary M. Herley, J. T. Heron, S. R. Hewitt, Rachel M. Hickinbotham, H. F. Hills, J. D. Holdsworth, J. A. G. Holt, P. D. James, R. Johnston, Daphne M. E. Kayton, R. G. M. Keeling, W. P. Kelly, R. F. S. Kirkham, Mary E. Larg, Helen M. J. Lawn, J. F. Leaver, Joyce R. Lewis, L. E. Lotimer, R. St. J. Lyburn, I. Macdonald, A. M. Mackenzie, T. E. L. J. McNair, J. D. H. Mahony, Dorothy M. Marshall, K. bin-M. O. Megat, Rene M. Michelmore, J. L. Middlemiss, P. D. V. Moni, Valerie N. Nairn, W. LeV. Needham, L. P. A. Newborne, T. A. O'Donnell, Ann K. O'May, D. G. O'Sullivan, H. P. L. Ozorio, L. J. Page, J. H. K. Parker, M. L. Paterson, A. S. S. Playfair, P. K. Pybus, B. O. Reed, Dorothy M. Ridout, D. A. Road, Joan M. Robinson, Heather J. S. Ross, H. A. Rowley, J. L. D. Roy, A. O. Sankey, E. Sheehan, Pamela M. Smith, J. A. Sodipo, T. A. Solomon, F. V. Squires, P. J. Stack, A. Starritt, J. Stohlner, Doreen M. J. Stracey, A. S. Subramani, Elaine M. Sunderland, W. F. Sunderland, W. D. G. Tellam, Dorothy E. M. Thomas, S. W. Thomson, G. M. Turner, R. N. H. Vann, L. Varma, A. S. Wallace, Alice M. Waters, P. Watson, P. W. Wells, P. Wen-chee Mao (Moore), D. B. B. Whitehouse, Edith J. Whitelaw, Alice R. E. Widdows, H. A. G. Winter, Ursula E. Zander, H. T. Zborowski.

CONJOINT BOARD IN SCOTLAND

The following candidates, having passed the final examinations, have been admitted L.R.C.P.Ed., L.R.C.S.Ed., L.R.F.P.&S.Glasg.:

D. S. Anderson, R. A. Atherton, G. J. Bagley, P. M. Brazil, P. Freeman, J. H. Gentles, H. Gerber, L. H. Geronimus, Susan MacA. Gillies, T. E. Grant, J. C. O. Iwenofu, J. Jochnowitz, A. Logan, L. C. Luck, K. E. M. Melville, M. Metz, A. W. P. Millard, A. J. Mone, W. McIlwraith, Monica B. Macnamara, Eleanor D. M. Pierce, D. Pride, R. F. Reid, Ellen M. Rosenthal, D. Simon, P. H. Slade, R. A. Spalding, Helen L. Steven, D. Stewart, J. A. Turner, R. Wilson, J. Winning, J. S. Wood, M. J. Zimmerman.

Dr. Thomas D. Dublin has been appointed executive director of the American National Health Council. For the last six years he has been professor of preventive medicine at the Long Island College of Medicine, Brooklyn. The National Health Council was founded in 1921 by a group of national health organizations. It has recently received a grant of $225,000 from the Rockefeller Foundation.

Medical News

Advisory Committee on Medical Nomenclature and Statistics

The Registrar-General has set up an Advisory Committee on Medical Nomenclature and Statistics. The function of the committee will be to consider from the medical point of view and to advise upon questions affecting the international statistical classification of diseases, injuries, and causes of death, and many other matters concerning medical nomenclature or statistics which may from time to time be referred to it. The chairman is Sir Ernest Rock Carling and the members are Sir Allen Daley, Professor Ernest Finch, Dr. F. H. K. Green, Dr. C. F. Harris, Professor A. Bradford Hill, Professor A. J. Lewis, Dr. A. Massey, Dr. P. L. McKinlay, Professor N. C. W. Nixon, Dr. W. N. Pickles, Dr. A. H. T. Robb-Smith, Dr. Percy Stocks, Professor R. E. Tunbridge, Sir Lionel Whitby, and Dr. A. Louise Winner. The secretary of the committee is Mr. L. M. Feery, General Register Office, Somerset House, London, W.C.2.

Industrial Health Research Board

The following have accepted the invitation of the Medical Research Council to serve as members of the Industrial Health Research Board during the next three years: Sir Frederic C. Bartlett, F.R.S. (chairman), Sir Charles J. Bartlett, Professor R. V. Christie, F.R.C.P., Mr. C. R. Dale, Dr. A. N. Drury, F.R.S., Sir Luke Fawcett, Professor T. Ferguson, M.D., Sir Claude Gibb, F.R.S., Professor A. Bradford Hill, Professor Esther M. Killick, M.R.C.P., Professor R. E. Lane, F.R.C.P., Dr. A. Massey, Dr. E. R. A. Merewether, Dr. J. M. Rogan, Dr. Donald Stewart, and Dr. Joan M. Faulkner (secretary). The Board is appointed by the Council to advise and assist it in that part of its research programme which relates to occupational health. The detailed consideration of research work is in the hands of scientific committees dealing with such subjects as occupational medicine, occupational physiology, occupational psychology, industrial pulmonary diseases, toxicology, and statistics. These committees report directly to the Council for purposes of immediate action. The function of the Board itself is that of a reviewing body considering general policy with regard to research over the whole field.

The Royal Society

At a meeting of the Royal Society, held on Nov. 30, the following officers were elected for the ensuing year: *President*, Sir Robert Robinson; *Treasurer*, Sir Thomas Merton; *Secretaries*, Sir Edward Salisbury and Professor D. Brunt; *Foreign Secretary*, Professor E. D. Adrian, O.M., M.D. Fifteen other Fellows were elected to the Council of the Society, including the following members of the medical profession: Professor G. R. Cameron, F.R.C.P., Dr. C. H. Kellaway, F.R.C.P., and Professor S. Zuckerman, M.D.

Higher Pay for Hospital Domestics

Agreement has been reached by the Ancillary Staffs Council of the Whitley Council for the Health Services (Great Britain) on revised rates of pay for domestic and manual workers in hospitals and institutions. They will also apply to residential establishments controlled by local authorities. The revised rates for the basic grades are 106s. for men and 82s. for women in London, 100s. for men and 75s. for women in urban areas, and 97s. for men and 74s. for women in rural areas. These new rates will in general result in increases ranging from 1s. to 8s. a week for men and from 2s. to 7s. a week for women, and are based on a 48-hour week. About 130,000 employees are affected.

Advisory Council on Child Care

The Home Secretary has appointed the Advisory Council on Child Care provided for in the Children Act. The members are: Professor Alan Moncrieff (chairman), Lady Allen of Hurtwood, Dr. Muriel Barton Hall, Mr. R. Beloe, Miss S. C. Bertie, Mrs. F. M. Brown, Mr. P. B. Dingle, Mrs. K. W. Jones-Roberts, Mr. P. T. Kirkpatrick, Mrs. Dermot Morrah, Miss L. M. Rendel, and Mr. David Smith. Departmental representatives of the Home Office and the Ministries of Education, Health, and Labour have also been appointed.

One Man's Story

"One Man's Story" is a film which has been produced for the Foreign Office by the Central Office of Information with the object of telling people, in this country and overseas, about British achievements in public health. It is a description of the work of the late Dr. G. C. M. M'Gonigle, who was medical officer of health for Stockton-on-Tees from 1925 until his death in 1939, and it illustrates the manifold duties which medical officers of health are called upon to perform. The film in particular brings out M'Gonigle's observation that in spite of the transfer of half the residents of a slum area in Stockton to a model housing estate their health did not show the

expected improvement, and at the end of five years the death rate was rising in spite of better housing. The simple reason was that the people, having to spend rather more on rent, spent rather less on food, and the lesson was driven home that social improvement was not to be brought about by attention to only one factor in the situation. The part of M'Gonigle in the film is taken by Murray Matheson, but apart from one other there are no professional actors in the film, the cast consisting of members of the council and citizens of Stockton, where nearly all the filming was done. Perhaps the desire not to make too long a film—it runs for only 26 minutes—has resulted in some aspects of M'Gonigle's work being passed over lightly. But it is a very human presentation. It brings out the two sides of a medical officer of health's work—the control of hygiene and the personal services. It is produced by the Horizon Film Unit in association with the Film Producers Guild, and Dr. M'Gonigle's successor at Stockton-on-Tees, Dr. H. J. Peters, has co-operated.

World Federation for Mental Health

The report of the International Preparatory Commission of the Congress on Mental Health, which met in London in August, has been issued under the title "Mental Health and World Citizenship." It is obtainable for 1s. (1s. 2d. post free) from the World Federation for Mental Health, 19, Manchester Street, London, W.1.

Literature of Food Investigation

The Department of Scientific and Industrial Research has issued the *Index to the Literature of Food Investigation*, Vol. 17, No. 1, June, 1945 (H.M.S.O. 6d.). Short notes on the contents of each article follow the reference to it.

Wills

Mr. Robert Ollerenshaw, of Didsbury, Manchester, left £104,071. Dr. Robert Haslam, of Bolton, left £24,823; Dr. Charles Albert Ernest Griffiths, of Meopham, Kent, £5,281; Dr. Charles Dainty Hatrick, of Hadley Wood, Middlesex, £5,081; and Surgeon Rear-Admiral James Herbert Fergusson, late R.N., £1,483.

COMING EVENTS

Congress of Comparative Pathology

Titles of papers to be presented at the Fifth International Congress of Comparative Pathology (Nov. 20, p. 923) at Istanbul should be sent by Dec. 15 to Mr R. E. Glover, Royal Veterinary College, London, N.W.1. The papers should be sent by Feb. 20, 1949, to Pr. N. R. Belger, Taksim, Siraserviler 75/3, Istanbul, Turkey.

SOCIETIES AND LECTURES

Monday

MEDICAL SOCIETY OF LONDON, 11, Chandos Street, Cavendish Square, W.—Dec. 13, 8.30 p.m. "*Therapeutic Application of Anticoagulants.*" Discussion to be introduced by Dr. Paul H. Wood and Mr. A. Dickson Wright.

Tuesday

CHADWICK TRUST.—At Royal Society of Tropical Medicine and Hygiene, 26, Portland Place, London, W., Dec. 14, 2.30 p.m. "*The Rise and Fall of the First General Board of Health,*" by Mr. S. E. Finer

CHELSEA CLINICAL SOCIETY.—At South Kensington Hotel, 47, Queens Gate Terrace, London, S.W., Dec. 14, 7 for 7.30 p.m. Discussion: "*Films and their Influence.*" To be opened by Mr. Sidney Gilliat (J. Arthur Rank organization).

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, Leicester Square, London, W.C.—Dec. 14, 5 p.m. "*Histopathology of the Skin,*" by Dr. I. Muende

INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., Dec. 14, 11 a.m., "*Cerebrospinal Fluid Tests for Syphilis,*" by Dr. R. Thomson; at St. Peter's Hospital, Henrietta Street, London, W.C., Dec. 14, 5 p.m., "*Congenital Defects of the Testicle and Epididymis,*" by Mr. Harland Rees.

PHYSIOTHERAPISTS ASSOCIATION OF GREAT BRITAIN.—At Charing Cross Hotel, Strand, London, W.C., Dec. 14, 8 p.m. "*Physical Medicine in Diseases of the Endocrine Glands,*" by Dr. A. P. Cawadias.

SOCIETY OF CHEMICAL INDUSTRY: FOOD GROUP, LONDON SECTION, AND AGRICULTURE GROUP.—At Main Chemistry Lecture Theatre, Royal College of Science, Imperial Institute Road, London, S.W., Dec. 14, 5.30 p.m. Joint meeting. Address: "*World Cereals To-day,*" by Mr. C. A. Loombe.

Wednesday

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, Leicester Square, London, W.C.—Dec. 15, 5 p.m. "*X-ray Technique,*" by Dr. C. W. McKenny.

INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., Dec. 15, 11 a.m., "*The Toxic Manifestations of Treatment in Syphilis,*" by Dr. W. N. Mascall; 5 p.m., "*Tumours of the Testicle,*" by Mr. W. K. Irwin.

Thursday

EDINBURGH CLINICAL CLUB.—At B.M.A. Scottish House, 7, Drumsheugh Gardens, Edinburgh, Dec. 16, 8 p.m. "*The Therapeutic Use of the Minerals,*" by Dr. A. G. Badenoch.

INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., Dec. 16, 11 a.m., "*The Toxic Manifestations of Treatment in Syphilis,*" by Dr. W. N. Mascall; at St. Peter's Hospital, Henrietta Street, London, W.C., Dec. 16, 5 p.m., "*Injuries and Disease of the Testicle and Epididymis, other than Tumour or Tuberculosis,*" by Mr. Harland Rees.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, London, S.W.—Dec. 16, 4.30 p.m. "*Neurology and Psychiatry.*" Lecture-demonstration by Dr. Anthony Feiling.

Friday

LONDON CHEST HOSPITAL, Victoria Park, E.—Dec. 17, 5 p.m. "*Clinical and Cardiographic Methods in the Diagnosis of Coronary Syndromes,*" by Dr. K. Shirley Smith.

MAIDA VALE HOSPITAL MEDICAL SCHOOL, Maida Vale, London, W.—Dec. 17, 5 p.m. Case demonstration by Dr. E. A. Blake Pritchard.

APPOINTMENTS

BRINDLE, T. W., M.B., Ch.B., Full-time Medical Officer for Central Area of Flintshire.

GEE, A. C., M.R.C.S., L.R.C.P., D.P.H., Medical Officer of Health, Lowestoft.

GRETTON-WATSON, B. G., M.B., B.Chir., D.P.H., Deputy Medical Officer of Health for Cheshire.

HOSPITAL FOR SICK CHILDREN, Great Ormond Street, London, W.C.—*Resident Assistant Physician*, D. N. Lawson, M.B., B.Chir., M.R.C.P. *House-physician*, F. S. W. Brimblecombe, M.B., B.S., M.R.C.P. *House-surgeon*, H. R. Jolly, M.B., B.Ch., M.R.C.P. *Supernumerary Medical Registrar*, F. W. Nash, M.B., B.S., M.R.C.P. *Supernumerary Registrar to Department of Physical Medicine*, D. C. Arnott, M.B., B.S., D.C.H.

RHYDWEN, R., D.S.C., M.B., B.S., D.P.H., Full-time Medical Officer for Western Area of Flintshire.

THOMPSON, B. A., M.R.C.S., L.R.C.P., Assistant Pathologist, Watford Peace Memorial Hospital, North-West Metropolitan Regional Hospital Board.

THORBURN, A. L., M.D., D.P.H., Divisional School Medical Officer and District Medical Officer of Health for the Urban and Rural Councils of Nantwich, Cheshire.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Child.—On Nov. 28, 1948, at the General Hospital, Newcastle-upon-Tyne, to Margot, wife of Dr. J. P. Child, a son.

Darcus.—On Nov. 27, 1948, at Churchill Hospital, Oxford, to Mary, wife of Howard Darcus, B.M., a son.

Ebbage.—On Nov. 29, 1948, at Highgate, to Margaret (née Cunnison), wife of Geoffrey Ebbage, a son—Ian.

Miller.—On Nov. 24, 1948, at Belfast, to Noël (née Gardiner), wife of Geoffrey Miller, M.R.C.P.I., Riversley, Banbridge, Co. Down, a daughter.

Smith.—On Dec. 1, 1948, at the Barratt Maternity Home, Northampton, to Sheila (née Macbriar), wife of Alastair W. Smith, M.B.E., L.R.C.P.&S.Ed., L.R.F.P.S.Glas., a daughter.

Stevenson.—On Nov. 28, 1948, at King's College Hospital, London, S.E., to Marjorie (née Ferguson Wood), wife of John Stevenson, M.R.C.S., L.R.C.P., a son.

DEATHS

Chambers.—On Nov. 23, 1948, at The Winnats, St. Helens, Isle of Wight, Wilfrid Metcalfe Chambers, M.D., aged 66.

Drew.—On Nov. 27, 1948, at White Lodge, Fleet, Charles Milligan Drew, D.S.O., M.B., Ch.B., retired Colonel, A.M.S., aged 68.

D'Rosario.—Recently, Wilfred James D'Rosario, M.R.C.S., L.R.C.P., of Carlisle, Cumberland

Ferguson.—On Nov. 28, 1948, at Braeside, Bishop Auckland, Co. Durham, Tom Entwisle Ferguson, L.R.C.P.&S.Ed., L.R.F.P.S.Glas.

Grove.—On Nov. 28, 1948, William Reginald Grove, M.D., of St. Ives, Hunts, aged 79.

Hamilton.—On Nov. 24, 1948, Louisa Hamilton, M.D., of Aylesbury, Bucks.

Lilley.—On Nov. 22, 1948, Ernest Lewis Lilley, F.R.C.S., of New Walk, Leicester, aged 72.

Linklater.—On Nov. 24, 1948, at City Hospital, Edinburgh, George James Irvine Linklater, O.B.E., M.D.Ed.

Macrae.—Recently, at Worcester, South Africa, Duncan Mackenzie Macrae, M.D.

Moncrieff.—On Dec. 1, 1948, at 8, Queen's Road, Hendon, London, N.W., Agnes Moncrieff, M.B., Ch.B.

Parsons.—On Dec. 4, 1948, at Nuffield House, Guy's Hospital, London, S.E., Frank Bett Parsons, M.D., F.R.C.P., of 77, Grange Road, Cambridge, aged 46.

Rawlings.—On Nov. 23, 1948, at Cambridge, Grahame Rigby Rawlings, M.B., B.Chir., late of Calcutta.

Reid.—On Nov. 29, 1948, at Ashleigh, Linthorpe, Middlesbrough, Yorks, John Bernard Reid, M.Ch., F.R.C.S.Ed., aged 48.

Rooke.—On Nov. 26, 1948, at Woodhouse, Headley, Newbury, Berks, Frederick James Faulkland Rooke, M.R.C.S., L.R.C.P., L.D.S., aged 77.

Scott.—On Dec. 1, 1948, at Craig-y-Barns, Frensham Vale, near Farnham, Surrey, John Livingstone Scott, M.B., Ch.B.

Sequeira.—Recently, in Kenya, James Harry Sequeira, M.D., F.R.C.P., F.R.C.S., aged 83.

Stuart.—On Nov. 26, 1948, at Westwood, Oakfield Road, Harpenden, Herts, Emily Gertrude Stuart, M.B., formerly of the C.E.Z.M.S. Hospital, Quetta, aged 76.

Topham.—On Nov. 28, 1948, at Folkestone, John Arthur Topham, M.R.C.S., L.R.C.P., formerly of Chartham, aged 74.

Whiteman.—On Sept. 23, 1948, John Wells Whiteman, M.R.C.S., L.R.C.P., aged 68.

No. 47

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended Nov. 20.

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for: (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

Disease	1948 (a)	1948 (b)	1948 (c)	1948 (d)	1948 (e)	1947 (Corresponding Week) (a)	1947 (Corresponding Week) (b)	1947 (Corresponding Week) (c)	1947 (Corresponding Week) (d)	1947 (Corresponding Week) (e)
Cerebrospinal fever	32	2	14	—	—	30	2	21	1	—
Deaths		—	—				—	1		
Diphtheria	154	14	58	11	3	220	23	46	23	2
Deaths	—	—	—	—	—	2	1	—	—	—
Dysentery	49	10	49	1	—	141	17	15	—	—
Deaths				—	—				—	—
Encephalitis lethargica, acute	—	—	—	—	—	3	—	—	—	—
Deaths		—					—			
Erysipelas			42	5	4			24	12	1
Deaths		—					—			
Infective enteritis or diarrhoea under 2 years				37					39	
Deaths	22	2	9	4	—	57	8	16	9	3
Measles*	6,923	135	153	69	54	2,233	120	178	258	5
Deaths†			1	—	—	2	—	3	1	—
Ophthalmia neonatorum	36	3	7	—	1	48	3	4	—	—
Deaths										
Paratyphoid fever	4	—	8 (B)	—	—	4	—	—	—	—
Deaths	—	—	—	—	—	—	—	—	—	—
Pneumonia, influenzal	732	52	1	3	5	503	31	5	2	4
Deaths (from influenza)‡	15	3	2	1	—	10	1	—	—	—
Pneumonia, primary			225	23				292	14	
Deaths	249	46		7	7		47		11	8
Polio-encephalitis, acute	6	—				3	1			
Deaths							1			
Poliomyelitis, acute	46	4	5	3	1	142	13	25	6	3
Deaths§	3	1					2			
Puerperal fever			2		—		1	8		—
Deaths										
Puerperal pyrexia‖	100	9	8	1	1	100	11	2	—	2
Deaths		—					—			
Relapsing fever	—	—			—	1	—			—
Deaths										
Scarlet fever	1,835	117	325	174	41	1,812	132	311	52	44
Deaths†			—	—	—	—	—	1	—	—
Smallpox	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Typhoid fever	9	2	1	4	1	3	—	—	5	—
Deaths	—	—	—	—	—	—	—	—	—	—
Typhus fever	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Whooping-cough*	2,680	168	110	68	8	1,183	86	46	31	2
Deaths	3	—	—	—	—	1	1	1	—	—
Deaths (0–1 year) Infant mortality rate (per 1,000 live births)	323	47	43	18	7	359	52	85	33	11
Deaths (excluding still-births)	5,063	846	647	168	117	4,822	799	684	197	142
Annual death rate (per 1,000 persons living)			13·1	10·5				14·2	12·4	
Live births	7,148	1107	880	364	237	7,465	1163	950	309	242
Annual rate per 1,000 persons living			17·8	22·8				19·1	19·5	
Stillbirths	222	27	29			198	37	34		
Rate per 1,000 total births (including stillborn)			32					35		

* Measles and whooping-cough are not notifiable in Scotland, and the returns are therefore an approximation only.

† Deaths from measles and scarlet fever for England and Wales, London (administrative county), will no longer be published.

‡ Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

§ The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, London (administrative county), are combined.

‖ Includes puerperal fever for England and Wales and Eire.

EPIDEMIOLOGICAL NOTES

Type "J" Typhoid Fever

There is reason to believe that three patients suffering from typhoid fever, one at Plaistow, one at Romford, and one at Lyme Regis, contracted the infection while *en route* from Australia to the United Kingdom, where they arrived in the first week of November. The organism responsible appears to belong to Vi phage type "J," which is not indigenous in England and Wales. It can be fairly assumed that type "J" infections appearing here at the present time come from a common source, and it is suggested that practitioners caring for patients suffering from typhoid should make a special effort to see that strains of the infecting organism reach the National Public Health Laboratory Service. M.Os.H. hearing of other patients who may be associated with the incident are asked to send details direct to S.M.O., Med. III, Ministry of Health, Whitehall.

Poliomyelitis in Iceland

An outbreak of infantile paralysis has occurred in Akureyri, in the North of Iceland. Up to Nov. 24, 160 cases had been reported, the majority in children. All schools in the town have been closed and public meetings forbidden. Mild outbreaks of "influenza" and "gastritis" are also reported from Akureyri.

Discussion of Table

In *England and Wales* an increase in the number of notifications was recorded for scarlet fever 385, whooping-cough 199, and acute pneumonia 153, and there was a decrease for dysentery 84 and acute poliomyelitis 14.

A small rise in the incidence of scarlet fever was reported from every region; the largest local rises were Lancashire 46 and Yorkshire West Riding 45. The largest fluctuations in the local trends of whooping-cough were increases in Southampton 39 and Warwickshire 38 and a decrease of 53 in Lancashire. Notifications of measles for the whole country increased by 13, but there were considerable variations in local returns; the largest increases were Yorkshire West Riding 103 and Durham 46, and the largest decreases were Derbyshire 130, Suffolk 64, and Lincolnshire 49. Only small changes were recorded in the local incidence of diphtheria. An increase of 37 in the notifications of acute pneumonia in Lancashire was the only change of any size in the local trends.

Of the 9 cases of typhoid fever 3 were notified in Liverpool C.B. No further cases of dysentery were notified from the outbreak in Essex, Hornchurch U.D., where 60 cases occurred last week. The largest returns of dysentery were Lancashire 12 and London 10. The largest returns of acute poliomyelitis were London 4, Middlesex 4, Gloucestershire 4, and Yorkshire West Riding 4.

In *Scotland* a rise occurred in the incidence of infectious diseases, and increases in the number of notifications were reported for measles 34, acute primary pneumonia 25, and scarlet fever 23. In the city of Aberdeen 6 further cases of paratyphoid fever were notified; this makes a total of 29 cases in the past three weeks. The notifications of diphtheria in the city of Glasgow were 5 more than in the preceding week.

In *Eire* rises occurred in the notifications of measles 19 and whooping-cough 12, while decreases were reported for scarlet fever 33 and diarrhoea and enteritis 17. An outbreak of measles affecting 26 persons was notified from Tipperary, Nenagh R.D. The decline in diarrhoea and enteritis was due to a fall of 17 in the number of notifications in Dublin C.B.

In *Northern Ireland* an increase of 8 was recorded in the notifications of measles from Belfast C.B.

Week Ending November 27

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 1,544, whooping-cough 2,747, diphtheria 141, measles 8,547, acute pneumonia 716, cerebrospinal fever 36, acute poliomyelitis 42, dysentery 72, paratyphoid 1, and typhoid 3.

Dr. C. H. Andrewes, F.R.S., who since 1927 has been a member of the Scientific Staff of the National Institute for Medical Research, left Britain recently to lecture in Hungary for the British Council on "The Common Cold" and "Recent Work on Influenza." Dr. Andrewes is in charge of the Medical Research Council's scientific investigations into the common cold at Salisbury and was one of the team which first isolated an influenza virus in 1933.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Lobeline and Asphyxia Neonatorum

Q.—*What is the value of an injection of lobeline in an asphyxiated newborn baby? Is it specific in these circumstances? If not, what percentage of success can be obtained?*

A.—Lobeline hydrochloride given by injection is reputed to stimulate the respiratory centre in the medulla and to increase its sensitivity to carbon dioxide. However, it cannot be regarded as a specific remedy for asphyxia neonatorum, its effect being very inconstant. Many authorities now doubt whether it is of any value at all, and American writers in particular are sceptical. It is argued—and there is some animal experimental work in support—that in severe anoxaemia the respiratory centre is incapable of being stimulated by lobeline, which in such circumstances may even be harmful. In these cases the real need is for oxygen. Even though such an extreme view is not widespread in this country it is generally recognized that the use of lobeline hydrochloride and other stimulants is of secondary importance in the treatment of asphyxia neonatorum. It should be added that traditional views on the action of lobeline hydrochloride are now disputed, and it is suggested that the drug increases respiration by exciting the carotid sinus reflex. Even if it has such an effect, however, it is admitted that this is both transient and variable.

Anaesthesia for Tonsillectomy

Q.—*What is the best method of anaesthesia for dissection of tonsils in children aged 4 to 8? I have used ethyl chloride, but the duration of anaesthesia is limited and not always sufficient.*

A.—A variety of anaesthetic techniques are in use for this operation. The commonest, and one that gives excellent results, is as follows. The child is given an injection of atropine, as well as a sedative consisting of a moderate dose of "seconal" or morphine. Anaesthesia is induced with ethyl chloride on an open mask followed by drop-ether. When the jaw is relaxed and the child is well under, the mouth is opened and the particular gag of the surgeon's choice inserted; anaesthesia is maintained by insufflation of ether vapour with air or oxygen into the mouth and pharynx. Dissection of tonsils in children is generally a short operation, and no difficulty will be encountered in keeping the child under by the means described. The shortness of the operation, the ease with which the larynx in a child of this age may be damaged, and the satisfactory anaesthesia obtained by insufflation of the vapour alone normally make the insertion of an endotracheal tube unnecessary, although some experienced anaesthetists do it as a routine.

Post-traumatic Neurosis

Q.—*Two years ago a man aged 42 hurt his back when lifting a bag of potatoes on to a cart. Three days later he found he could not walk without pain. No x-ray evidence of damage has been found, and the patient has been pronounced neurasthenic. Under narcosis he shows no conflict whatever regarding compensation, etc. He drags his left leg after him, refusing to bend ankle or knee-joint. What further treatment do you suggest? Might repeated intravenous narcosis with suggestion succeed?*

A.—The writer is not wholly satisfied from the description given that the case is necessarily neurotic. The exclusion of organic causes by *x* rays is of course important and necessary, but the prevalent habit of diagnosing a case as neurotic simply on the grounds that no organic condition is found should be resisted. The fact that an organic cause cannot be found does not always mean there is not one. No doubt before the discovery of the vitamins many cases of depression due to vitamin deficiency were treated as psychogenic because no organic cause could be found. Neurotic and hysteric conditions are to be diagnosed on positive as well as negative grounds, and the patient's psychological history and his personal problems, conscious and unconscious, at the time of the trauma, as well as the events of the accident, must be investigated. In this case one such positive factor has rightly been taken into consideration—that of compensation. But there may be other reasons for resorting to a hysteric symptom. In the occupational neuroses, for instance, there is a latent desire to escape from work which the patient finds uncongenial but which he is compelled to do either from necessity or from some moral obligation. (Telephone-girl's deafness and the "war neuroses" of soldiers are instances of such occupational neuroses.) But there are many other problems of an infinitely more complicated nature which may be at the bottom of the neurosis (if this is one).

Repeated suggestion under narcosis may be of service, but it has the weakness of all suggestive treatment—namely, that it may be working against the patient's unconscious wish to be ill, as in the occupational neuroses. It is a case of the physician's suggestion *versus* the more deeply rooted autosuggestion of the patient. The number of treatments therefore depends on the strength of the unconscious resistance of the patient against cure, as well as on the toxicity of the drugs. Analysis under drugs we should expect to give the better results, since emotional problems often emerge under narcosis; but this is by no means an infallible method, and often draws a blank. In any case, the patient should be left to reveal his own problems, even under narcosis. If that fails, analysis under free association by an expert medical psychologist, which is longer but surer than the other methods, should be resorted to, if such treatment can be obtained.

Syringing Ears

Q.—*Is there any contraindication to the use of soap substitutes in syringing ears for wax?*

A.—There is no contraindication to the use of soap substitutes, but these are not necessary. Plain warm water is quite effective, provided it is directed along the postero-superior meatal wall, when quite a powerful jet will cause no discomfort. Bicarbonate of soda may usefully be added to the water.

Cysts of the Breast

Q.—*A woman of 44 has had cysts in her right breast for three or four years. They are not adherent to any tissue. Lately they have become somewhat harder on palpation. Could dienoestrol, which is being taken for menopausal disorders, in any way affect the pathology of the cysts? Would surgery be advisable?*

A.—If the cysts are part of what is known as chronic mastitis, the condition would be aggravated by dienoestrol and ameliorated by testosterone. As some of the nodules are said to become harder on palpation, a surgical opinion on their innocence should be sought. Should malignancy be excluded, it is probable that surgery would not be called for. On the history malignancy seems unlikely.

Stammering

Q.—*My small son, aged 3½, has recently developed a bad stammer. This is getting worse. There appears to be no mental conflict and he is healthy and happy. He is an only child of rather above average intelligence, and he is more right-handed than left-handed. He has not heard anyone else stammer, and playing with other children makes no difference. Is this a phase which will pass? If not, what steps can I take to cure the condition before it becomes well established?*

A.—It is difficult to be sure about the cause of the stammer in this case without knowing more of the factors associated with its onset. It might be connected with some change in the child's life, such as starting a nursery school or an alteration in the environment. It may also be that his ideas are outrunning his verbal powers, so that he thinks more quickly than he can speak. One may detect the latter condition by noticing the kind of stammer, which would probably be of the repetitive type, as if he were "tumbling over his words." If so, it would help him if he were spoken to slowly and in as simple language as possible. He might also learn to use speech more comfortably by associating this with rhythm in rhymes and songs. If his

stammer is of the blocking, explosive type he should see a speech therapist, and should do so in any case if the stammer does not clear up within the next few months.

Arterial Disease

Q.—*What drugs have any effect on endarteritis or atheroma in a man of 62 with normal blood pressure and electrocardiogram, and with a negative Wassermann reaction? He has pain over the carotid and bronchial arteries but negligible angina.*

A.—Points which need to be considered are: the aetiology, position, and extent of the endarteritis, the location of the atheroma, and whether the pain is spontaneous or occurs on pressure or with exercise. Unless endarteritis is due to syphilis or chronic suppurative lesions, we know of no drug that will affect it. Similarly, there is no known therapeutic agent for atheroma. The circulation can be improved by coronary vasodilators and undue cardiac strain avoided by limiting exercise to the point of anginal pain or breathlessness.

Delousing Heads by "T.I.F.A."

Q.—*I recently read an American article describing the Todd insecticide fog-applicator ("T.I.F.A."). Could you tell me if anything comparable to this machine exists in this country, and, if so, its approximate cost? I contend that children with pediculosis capitis might be passed through a room containing a suitable proportion of D.D.T. fog applied with the T.I.F.A., or the like, at regular intervals. Could I have your advice?*

A.—The T.I.F.A. fog insecticide disperser has been tested in this country but, so far as we are aware, is not manufactured here. It is a rather wasteful method of dispersing very large quantities of insecticide rapidly and over large areas. It might have advantages in large-scale field treatments, where, for example, it is desired to eradicate tsetse flies from large areas of African bush or to destroy rapidly all the mosquitoes in a small town or a large camp site. It is difficult to see why one should employ such a large, elaborate machine for the exceedingly simple procedure of applying insecticide to verminous heads. Several excellent preparations are available, such as "lethane special" (*British Medical Journal*, 1942, **1**, 464), D.D.T. emulsion (ibid., 1945, **1**, 409), or gamma-B.H.C. (*Med. Officer*, March 20, 1948). All of these are better applied by hand than by a fog in the air.

Care of the Hair and Scalp

Q.—(*a*) *What happens to the hair and scalp if left unwashed for a long time, say two years?* (*b*) *Is water or washing inimical to the health of the hair?* (*c*) *What are the most healthy materials for washing hair?* (*d*) *What is the best treatment for dandruff?*

A.—(*a*) Provided brushes and combs are washed frequently, and the hair is well brushed daily, a healthy scalp and hair need not be washed for years.

(*b*) Hard water and alkaline soaps are not good for the hair; with proper care there is no objection to frequent washing. This is not advisable except where the hair is very oily or the scalp has much dandruff.

(*c*) Rain water, soft water, and any good soap are best for the purpose. For the many methods which are harmless consult a book on dermatology.

(*d*) Dandruff (pityriasis capitis) is too big a problem to answer without examining the patient. If left alone, the next stages—pityriasis steatoides and circinata, with redness, exudation, and crusting—may develop. For simple dandruff use salicylic acid, gr. 8 (0.52 g.) and/or liquor carbonis detergens, ½ to 1 drachm (1.8 to 3.5 ml.) to the ounce (28.4 ml.) of industrial spirit, and water, equal parts. Some respond better to mercurial preparations. For severe cases the same drugs may be used in ointment form.

Penicillin and Tuberculosis

Q.—*Tuberculous abscesses after penicillin injections have been described. Is the incidence of tuberculous infection following penicillin injection higher than after other types of injection? Does penicillin favour the growth of Mycobacterium tuberculosis?*

A.—When tuberculous abscesses have resulted from therapeutic injections they have usually been due to the use of a contaminated syringe. The kind of material injected is likely to be of little consequence if it contains living tubercle bacilli, and presumably this occurrence is not so common that the incidence of tuberculous infection after penicillin and other injections can be compared statistically. According to Ungar and Muggleton (*J. Path. Bact.*, 1946, **58**, 501) penicillin stimulates the growth of *Myco. tuberculosis* in culture. Rivière, Thély, and Gautron (*C. R. Acad. Sci., Paris*, 1947, **224**, 1856) have reported that penicillin treatment accelerates death from tuberculosis in the guinea-pig; and Hauduroy and Rosset (*Ann. Inst. Pasteur*, 1948, **75**, 67), who have repeated these experiments, believe such deaths to be caused simply by penicillin itself, which is far more toxic to guinea-pigs than to any other animal.

NOTES AND COMMENTS

Ulceration of Mucous Membranes.—Dr. JAMES M. CANNING (Mitcham, Surrey) writes: With reference to the above subject, on which questions and answers have previously appeared in the *Journal* ("Any Questions?" Aug. 21, p. 408; March 15, 1947, p. 365; June 15, 1946, p. 940; Dec. 25, 1943, p. 839), I should like to advance a suggestion which may in some cases be of assistance to those practitioners who have had the disconcerting experience of endeavouring to alleviate this notorious and frequently quite intractable malady. I have observed within the past two months a definite and very dramatic improvement in three cases of recurrent ulceration of mucous membranes from the exhibition of "benadryl." In all three cases, which were female, the ulcers appeared chiefly on the mucous membranes of the mouth, tongue, gums, and fauces, and in these sites the lesions were either identical with or very similar to those described as recurrent aphthous or vesicular stomatitis. In each case the well-known menstrual exacerbation was noted; in two cases the lesions appeared simultaneously on the vaginal and labial mucosa, and in one case there was a co-existing idiopathic erythema multiforme affecting chiefly the anterior surfaces of both lower limbs. The patients had previously been treated at various times with vitamins and tonics, intravenous arsenicals, chorionic gonadotrophin, mouth washes, and local chemical cauterization, with very disappointing results. The use of benadryl was instituted having in mind the recent suggestion advanced by Zondek and Bromberg (*J. Obstet. Gynaec. Brit. Emp.*, 1947, **54**, 1) that the condition may sometimes be an allergic manifestation to one or other hormone. The initial dose of the drug employed was 200 mg. daily; in each case relief of local pain and tenderness was observed in 24–36 hours, and the ulcers had disappeared within 4–6 days, returning in 1–3 days after withdrawal of the drug; the lesions have since been held in abeyance by an arbitrary dose of—at present—50 mg. daily. In these cases familial manifestations of allergy (bronchial asthma, paroxysmal rhinorrhoea) could be traced, and it may well be that the mucosal lesions were an unusual expression of an otherwise clinically dormant allergic diathesis.

D.F.P.—With reference to our annotation (Oct. 16, p. 719) on the subject of abdominal distension and D.F.P., Messrs. Allen and Hanburys, Ltd. (Ware, Herts), inform us that they supply a sterile 0.1% solution of D.F.P. in arachis oil for intramuscular injection, and 0.05 and 0.1% solutions in sterile arachis oil for ophthalmic use. The allied anticholinergic drug, tetraethylpyrophosphate (T.E.P.P.), can also be supplied for parenteral and oral administration.

Corrections

Sir HENRY DALE writes: In my opening statement at a discussion on the physiological basis of neuromuscular disorders, at the Annual Meeting at Cambridge, a sentence on p. 890 of your issue of Nov. 20 (line 19) begins: "It is incompatible, accordingly . . . etc." The passage should read: "It is compatible, accordingly . . ."

Dr. J. M. RUSSELL, Divisional Medical Officer of Health for the West Riding of Yorkshire, refers to 12 cases of diphtheria notified as from Hoyland Nether Urban District ("Epidemiological Notes," Dec. 4, p. 1004). This is an error which has now been corrected by the Registrar-General. In the Weekly Returns of Infectious Diseases for the week ending Nov. 13 sent to the Registrar-General the figure 12 appeared under the heading "Diphtheria" instead of in the next column headed "Measles."

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